DESCRIPTION

TRICYCLIC BENZOPYRAN COMPOUND AS ANTI-ARRHYTHMIC AGENTS

Technical Field

The present invention relates to benzopyran derivatives having the prolongation effect on the refractory period, which are used for the treatment of arrhythmia in mammals including human being.

Background Art

As benzopyran derivatives, 4-acylaminobenzopyran derivatives exemplified by Cromakalim have been known (for example, Japanese Patent Laid-open No. Sho 58-67683). These 4-acylaminobenzopyran derivatives exemplified by Cromakalim are known to open ATP sensitive K⁺ channel so as to be effective for the treatment of hypertension and asthma, but there has not been any mention as to the treatment of arrhythmia based on the prolongation effect on the refractory period.

In addition, it is reported that 4-aminobenzopyran derivatives that have β 3-receptor stimulating action are supposed to be effective for the treatment of corpulence (for example, WO 03/014113), but there has not been any mention as to the treatment of arrhythmia based on the prolongation effect on the refractory period in this document.

Disclosure of Invention

In the meanwhile, conventional anti-arrhythmic agents having the prolongation effect on the refractory period as a main mechanism (such as Class I drugs of anti-arrhythmic agent classification according to Vaughan Williams, or d-sotalol or dofetilide belonging to Class III) have the therapeutic problems in inducing highly dangerous arrhythmia leading to the sudden death from such as *torsades de pointes* among others due to prolongation of action potential in ventricular muscle correlated to the prolongation effect on the refractory period. Thus, treating agents with less adverse effect have been highly desired.

The inventors have investigated compounds having the prolongation effect on the refractory period selective for atrium muscle rather than for ventricular muscle in order to solve the problems, and consequently found that the compound of formula (I) or (II) has the prolongation effect on the refractory period selective for atrium muscle

without any influence on the refractory period and action potential in ventricular muscle. Thus, the present invention has been accomplished.

That is, the present invention relates to the following aspects:

(1) A benzopyran derivative of formula (I) or (II), or pharmaceutically acceptable salt thereof

wherein

 R^1 and R^2 are independently of each other hydrogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), or C_{6-14} aryl group (wherein the aryl group may be arbitrarily substituted with halogen atom, hydroxy group, nitro group, cyano group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group) or C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom));

 R^3 is hydroxy group or C_{1-6} alkylcarbonyloxy group, or R^3 forms a bond together with R^4 :

 R^4 is hydrogen atom, or R^4 forms a bond together with R^3 ;

m is an integer of 0 to 4;

n is an integer of 0 to 4;

V is a single bond, CR^7R^8 wherein R^7 is

- C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group, C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} is halogen atom; hydroxy group; C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom)); C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom); nitro group; cyano group; formyl group; formamide group; sulfonylamino group;

sulfonyl group; amino group; C_{1-6} alkylamino group; di- C_{1-6} alkylamino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; carboxy group or C_{6-14} arylcarbonyl group, and when a plurality of R^{10} are present, they may be identical or different from each other); C_{1-6} alkylcarbonyloxy group; nitro group; cyano group; formyl group; formamide group; amino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminosulfonyl group; C_{1-6} alkylsulfonyl group; C_{1-6} alkylsulfon

- C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} has the above-mentioned meaning);
- hydroxy group;
- C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom); or
- nitro group; cyano group; formyl group; formamide group; sulfonylamino group; sulfonyl group; amino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminosulfonyl group; C_{1-6} alkylaminosulfonyl group; C_{1-6} alkylaminosulfonyl group; carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} has the above-mentioned meaning), and R^{8} is
- hydrogen atom,
- C_{1-6} alkyl group (wherein the C_{1-6} alkyl group may be arbitrarily substituted with halogen atom, hydroxy group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), C_{1-6} alkylcarbonyloxy group; nitro group; cyano group; formyl group; formamide group; amino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group;

di- C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylcarbonyl group; C_{1-6} alkoxycarbonyl group; aminosulfonyl group; C_{1-6} alkylsulfonyl group; carboxy group or sulfonyl group); - C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10});

- hydroxy group;
- C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or
- nitro group; cyano group; formyl group; formamide group; sulfonylamino group; sulfonyl group; amino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; C_{1-6} alkylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylaminosulfonyl group; C_{1-6} alkylaminosulfonyl group; C_{1-6} alkylaminosulfonyl group; C_{1-6} alkylaminosulfonyl group; carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), or

R⁷ together with R⁸ may represent =O or =S, or

V is NR⁹ wherein R⁹ is hydrogen atom, C₁₋₆ alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), hydroxy group, C₆₋₁₄ aryl group, C₂₋₉ heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), C_{1-6} alkylaminocarbonyl group, di- C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C₃₋₈ cycloalkylcarbonyl group, C₁₋₆ alkoxycarbonyl group, C₁₋₆ alkylsulfonyl group, carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group), C_{1-6} alkylaminocarbonyl group, di-C₁₋₆ alkylaminocarbonyl group, C₁₋₆ alkylcarbonyl group, C₃₋₈ cycloalkylcarbonyl group, C₁₋₆ alkoxycarbonyl group, C₁₋₆ alkylsulfonyl group, C_{6-14} arylsulfonyl group, C_{2-9} heteroarylsulfonyl group (wherein each of the arylsulfonyl group or heteroarylsulfonyl group may be arbitrarily substituted with 1 to 3 R^{17} wherein R^{17} has the same meaning as R^{10}), carboxy group; C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R¹⁷ wherein R¹⁷ has the same meaning as R¹⁰); or

V is O, S, SO or SO₂;

 $\ensuremath{\mathsf{R}}^5$ is hydrogen atom or $\ensuremath{\mathsf{C}}_{1\mbox{-}6}$ alkyl group (wherein the alkyl group may be arbitrarily

substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group); and R^6 is

- hydrogen atom,
- C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group),
- C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group),
- amino group, C_{1-6} alkylamino group, di- C_{1-6} alkylamino group, C_{6-14} arylamino group, C_{2-9} heteroarylamino group (wherein each of the arylamino group or heteroarylamino group may be arbitrarily substituted with 1 to 3 R¹⁸ wherein R¹⁸ has the same meaning as R¹⁰);
- C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10}); or
- C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the above-mentioned meaning), hydroxy group, nitro group, cyano group, formyl group, formamide group, amino group, C_{1-6} alkylamino group, di- C_{1-6} alkylamino group, C_{1-6} alkylamino group, aminocarbonyl group, C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylaminocarbonyl group, carboxy group or C_{6-14} arylcarbonyl group);
- A is 5-, 6- or 7-member ring fused with benzene ring (wherein the 5-, 6- or 7-member

ring may be arbitrarily substituted with 1 to 6 R²¹ wherein R²¹ has the same meaning as R¹⁰, and when a plurality of R²¹ are present, they may be identical or different from each other), as constituent atom of the ring, oxygen atom, nitrogen atom or sulfur atom may be contained in the number of 1 to 3 alone or in a combination thereof, the number of unsaturated bond in the ring is 1, 2 or 3 including an unsaturated bond of the benzene ring to be fused, carbon atoms constituting the ring may be carbonyl or thiocarbonyl;

(2) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (1), wherein A is

wherein R^{11} and R^{12} are independently of each other hydrogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy

group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), hydroxy group, C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R¹⁹ wherein R¹⁹ has the same meaning as R¹⁰), C₁₋₆ alkylaminocarbonyl group, di-C₁₋₆ alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{3-8} cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group), C_{6-14} aryl group, C_{2-9} heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R¹⁹ wherein R^{19} has the same meaning as R^{10}), C_{1-6} alkylaminocarbonyl group, di- C_{1-6} alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{3-8} cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, C_{6-14} arylsulfonyl group, C_{2-9} heteroarylsulfonyl group (wherein each of the arylsulfonyl group or heteroarylsulfonyl group may be arbitrarily substituted with 1 to 3 R¹⁹ wherein R¹⁹ has the same meaning as R¹⁰), carboxy group; C₆₋₁₄ arylcarbonyl group or C₂₋₉ heteroarylcarbonyl group (wherein each of the arylcarbonyl group or heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R¹⁹ wherein R¹⁹ has the same meaning as R¹⁰), R¹³, R¹⁴, R¹⁵ and R¹⁶ are independently of each other hydrogen atom, halogen atom, C₁₋₆ alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, hydroxy group, C₆₋₁₄ aryl group, C₂₋₉ heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), C_{1-6} alkylaminocarbonyl group, di-C₁₋₆ alkylaminocarbonyl group, C₁₋₆ alkylcarbonyl group, C₃₋₈ cycloalkylcarbonyl group, C_{1-6} alkoxycarbonyl group, C_{1-6} alkylsulfonyl group, carboxy group, C_{6-14} arylcarbonyl group or C_{2-9} heteroarylcarbonyl group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), carboxy group, amino group, hydroxy group, C₆₋₁₄ aryl group or C₂₋₉ heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10})), C_{1-6} thioalkoxy group (wherein the thioalkoxy group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), carboxy group, hydroxy group, C₆₋₁₄ aryl group or C₂₋₉ heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R²⁰ wherein R^{20} has the same meaning as R^{10})), hydroxy group, C_{6-14} aryl group, C_{2-9} heteroaryl

group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), C_{1-6} alkylcarbonyloxy group, nitro group, cyano group, formyl group, formamide group, amino group, sulfonyl group, C₁₋₆ alkylamino group, di-C₁₋₆ alkylamino group, C₆₋₁₄ arylamino group, C_{2-9} heteroarylamino group (wherein each of the arylamino group or heteroarylamino group may be arbitrarily substituted with 1 to 3 R²⁰ wherein R²⁰ has the same meaning as R^{10}), C_{1-6} alkylcarbonylamino group, C_{1-6} alkylsulfonylamino aminocarbonyl group, C_{1-6} alkylaminocarbonyl group, alkylaminocarbonyl group, C_{1-6} alkylcarbonyl group, C_{6-14} arylcarbonyl group, C_{2-9} each of the arylcarbonyl group or heteroarylcarbonyl (wherein group heteroarylcarbonyl group may be arbitrarily substituted with 1 to 3 R^{20} wherein R^{20} has the same meaning as R^{10}), C_{1-6} alkoxycarbonyl group, aminosulfonyl group, C_{1-6} alkylsulfonyl group, C_{6-14} arylsulfonyl group, C_{2-9} heteroarylsulfonyl group (wherein each of the arylsulfonyl group or heteroarylsulfonyl group may be arbitrarily substituted with 1 to 3 R²⁰ wherein R²⁰ has the same meaning as R¹⁰), carboxy group, sulfonyl group or C₂₋₉ heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C₁₋₆ alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C₆₋₁₄ aryl group, C₂₋₉ heteroaryl group (wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R²⁰ wherein R²⁰ has the above-mentioned meaning), hydroxy group, nitro group, cyano group, formyl group, formamide group, amino group, C₁₋₆ alkylamino group, di-C₁₋₆ alkylamino group, C_{1-6} alkylcarbonylamino group, C_{1-6} alkylsulfonylamino group, aminocarbonyl group, C_{1-6} alkylaminocarbonyl group, di- C_{1-6} alkylaminocarbonyl group, C₁₋₆ alkylcarbonyl group, C₁₋₆ alkoxycarbonyl group, aminosulfonyl group, C₁₋₆ alkylsulfonyl group, carboxy group or C₆₋₁₄ arylcarbonyl group),

X is O, S, SO or SO₂;

- (3) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (2), wherein R^1 and R^2 are methyl group, R^3 is hydroxy group, and R^4 is hydrogen atom;
- (4) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein R⁵ is hydrogen atom, m is an integer of 0 to 3 and n is an integer of 0 to 2;

(5) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein V is a single bond;

- (6) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{6-14} aryl group wherein the aryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10} ;
- (7) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (6), wherein m is 2;
- (8) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (7), wherein R^6 is C_{6-14} aryl wherein the aryl group may be arbitrarily substituted with 1 to 3 halogen atom or amino group, and when a plurality of substituents are present, they may be identical or different from each other;
- (9) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{2-9} heteroaryl group wherein the heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10} ;
- (10) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (9), wherein m is 2;
- (11) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (10), wherein R⁶ is 2-pyridyl group, 3-pyridyl group or 4-pyridyl group;
- (12) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{2-4} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group), or C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom), C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom), C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkyl group may be arbitrarily substituted with halogen atom), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or

hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), hydroxy group or amino group);

- (13) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (12), wherein m is 2;
- (14) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (13), wherein R⁶ is n-propyl group, i-propyl group, c-pentyl group, c-hexyl group, 1-c-pentenyl group, 2-c-pentenyl group, 3-c-pentenyl group, 1-c-hexenyl group, 2-c-hexenyl group;
- (15) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein V is CR⁷R⁸;
- (16) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (15), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{1-6} alkylamino group, di- C_{1-6} alkylamino group, or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or R^7 and R^8 together are =O or =S;
- (17) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (16), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group) or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group), or R^7 and R^8 together are =0;
- (18) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (17), wherein R^7 is hydroxy group, and R^8 is hydrogen atom;
- (19) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (15), wherein m is an integer of 1 to 2, n is 0, and R^6 is C_{6-14} aryl group or C_{2-9} heteroaryl group wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10} ;
- (20) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (19), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the

alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{1-6} alkylamino group, di- C_{1-6} alkylamino group, or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or R^7 and R^8 together are =O or =S;

- (21) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (20), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group) or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group), or R^7 and R^8 together are =0;
- (22) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (21), wherein R⁷ is hydroxy group, and R⁸ is hydrogen atom;
- (23) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (22), wherein m is 1, n is 0, and R^6 is C_{6-14} aryl group wherein the aryl group may be arbitrarily substituted with 1 to 3 halogen atom or amino group, when and when a plurality of substituents are present, they may be identical or different from each other;
- The benzopyran derivative or pharmaceutically acceptable salt thereof as set (24)forth in (15), wherein m is an integer of 1 to 2, n is 0, and R^6 is C_{1-4} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{3-8} cycloalkyl group, C_{3-8} cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino, carboxy group or hydroxy group), or C₂₋₉ heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C₁₋₆ alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C₁₋₆

alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group);

- (25) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (24), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), C_{1-6} alkylamino group, di- C_{1-6} alkylamino group, or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or R^7 and R^8 together are =0 or =5;
- (26) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (25), wherein R^7 is hydroxy group, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group) or carboxy group, and R^8 is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or carboxy group), or R^7 and R^8 together are =0;
- (27) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (26), wherein R^7 is hydroxy group, and R^8 is hydrogen atom;
- (28) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (27), wherein R₀⁶ is n-propyl group, i-propyl group, c-pentyl group, c-hexyl group, 1-c-pentenyl group, 2-c-pentenyl group, 3-c-pentenyl group, 1-c-hexenyl group, 2-c-hexenyl group;
- (29) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (15), wherein R^7 and R^8 together are =0 or =S, and R^6 is amino group, C_{1-6} alkylamino group, di- C_{1-6} alkylamino group, C_{6-14} arylamino group or heteroarylamino group (wherein each of the arylamino group or heteroarylamino group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10}), or C_{2-9} heterocyclyl group (wherein the heterocyclyl may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy

group);

(30) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein V is NR⁹;

- (31) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (30), wherein m is an integer of 1 to 3, n is 0, and R^6 is C_{6-14} aryl group or C_{2-9} heteroaryl group wherein each of the aryl group or heteroaryl group may be arbitrarily substituted with 1 to 3 R^{18} wherein R^{18} has the same meaning as R^{10} ;
- (32) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (31), wherein m is 2;
- The benzopyran derivative or pharmaceutically acceptable salt thereof as set (33)forth in (30), wherein m is an integer of 1 to 3, n is 0 and R^6 is hydrogen atom, C_{2-4} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C₃₋₈ cycloalkyl group, C₃₋₈ cycloalkenyl group (wherein the cycloalkyl group or cycloalkenyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), or C_{2-9} heterocyclyl group (wherein the heterocyclyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C₁₋₆ alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group, carboxy group or hydroxy group);
- (34) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (33), wherein m is 2;
- (35) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), which is the compound of formula (I);
- (36) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), which is the compound of formula (II);
- (37) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is

wherein R¹¹, R¹³, R¹⁴ and R¹⁵ have the above-mentioned meanings;

- (38) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (37), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), and R^{13} , R^{14} and R^{15} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{3-8} cycloalkyl group (wherein the cycloalkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), C_{1-6} alkoxyl group (wherein the alkoxyl group may be arbitrarily substituted with halogen atom) or hydroxy group or hydroxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkylcarbonyl group, amino group, amino group, carboxy group or cyano group;
- (39) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (38), wherein R_{\downarrow}^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and R_{\downarrow}^{13} , R_{\downarrow}^{14} and R_{\downarrow}^{15} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), carboxy group, amino group or cyano group;
- (40) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (39), wherein R^{11} is hydrogen atom, R^{13} is hydrogen atom, halogen atom, carboxy group or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), R^{14} is hydrogen atom, and R^{15} is hydrogen atom, halogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group);
- (41) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is

wherein R¹¹, R¹², R¹³ and R¹⁴ have the above-mentioned meanings;

- (42) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (41), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), and R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group), C_{1-6} alkylcarbonyl group, amino group or cyano group;
- (43) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (42), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), amino group or cyano group;
- (44) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (43), wherein R¹¹, R¹², R¹³ and R¹⁴ are hydrogen atom;
- (45) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is

wherein R¹¹, R¹³ and R¹⁴ have the above-mentioned meanings;

(46) The benzopyran derivative or pharmaceutically acceptable salt thereof as set

forth in (45), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), amino group or hydroxy group), R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group), amino group or cyano group, and X is O, S, SO or SO_2 ;

- (47) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (46), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and X is O;
- (48) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (47), wherein R^{11} is hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), R^{13} and R^{14} are hydrogen atom, and X is O;
- (49) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (8), (11), (14), (23), (28) or (35), wherein the ring structure of A is

wherein R¹¹, R¹², R¹³ and R¹⁴ have the above-mentioned meanings;

(50) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (49), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group (wherein the aryl group may be arbitrarily substituted with halogen atom, hydroxy group or C_{1-6} alkoxy group (wherein the alkoxy group may

be arbitrarily substituted with halogen atom)), amino group or hydroxy group), and R^{13} and R^{14} are independently of each other hydrogen atom, halogen atom, C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom) or hydroxy group), C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom, amino group, C_{1-6} alkoxy group (wherein the alkoxy group may be arbitrarily substituted with halogen atom), or hydroxy group), amino group or cyano group;

- (51) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (50), wherein R^{11} and R^{12} are independently of each other hydrogen atom or C_{1-6} alkyl group (wherein the alkyl group may be arbitrarily substituted with halogen atom, amino group or hydroxy group), and R^{13} and R^{14} are hydrogen atom;
- (52) A benzopyran derivative or pharmaceutically acceptable salt thereof which is 2,2,7,9-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinol ine-7-carbonitrile,
- 3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinol ine-7-carboxamide,
- {3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-7-yl}ethanone,
- 3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2-ol, 7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol.
- 3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinol ine-7-carboxylic acid,
- $4-(benzylamino)-7-chloro-2,2,9-trimethyl-3,4-dihydro-2\emph{H}-pyrano[2,3-g]quinolin-3-ol, \\ 4-\{[(1,3-benzodioxol-5-yl)methyl]amino\}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2\emph{H}-pyrano[2,3-g]quinolin-3-ol, \\ 0[2,3-g]quinolin-3-ol, \\ 0[2,3-g]quinolin$
- 7-chloro-2,2,9-trimethyl-4-[(3-phenylpropyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol.
- 7-chloro-4- $\{[2-(4-fluorophenyl)ethyl]amino\}-2,2,9-trimethyl-3,4-dihydro-2$ *H*-pyrano[2,3-g]quinolin-3-ol,

7-chloro-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,

- 7-chloro-4-{[2-(4-chlorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 4-{[2-(4-aminophenyl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- $\label{eq:continuous} 7-chloro-4-[(2-hydroxy-2-phenylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2\textit{H}-pyrano[2,3-g]quinolin-3-ol,$
- 7-chloro-2,2,9-trimethyl-4-[(2-phenylbutyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol,
- 4-{[2-(1,3-benzodioxol-5-yl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyran o[2,3-g]quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(1-piperidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g] quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol,
- 4-[(2-anilinoethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol,
- 7-chloro-4-({2-[ethyl(3-methylphenyl)amino]ethyl}amino)-2,2,9-trimethyl-3,4-dihydro-2 *H*-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-4-{[(1-ethyl-(R)-2-pyrrolidinyl)methyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-4-[(2,2-diethoxyethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(3-thienyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(1-pyrazolyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]q uinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(4-methylpyrazol-1-yl)ethyl]amino}-3,4-dihydro-2*H*-pyran o[2,3-g]quinolin-3-ol,
- 7-chloro-4-{[2-(4-chloropyrazol-1-yl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyran o[2,3-g]quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(2-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(3-pyridyl)ethyl]amino}-3,4-dihydro-2H-pyrano[2,3-g]quin

olin-3-ol,

 $7-chloro-2,2,9-trimethyl-4-\{[2-(4-pyridyl)ethyl\}amino\}-3,4-dihydro-2\textit{H-pyrano}[2,3-g]quinolin-3-ol,$

7-chloro-4-ethylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,

7-chloro-4-isobutylamino-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol,

7-chloro-4-[(cyclopropylmethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]qui nolin-3-ol,

7-chloro-4-isopentylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 7-chloro-4-[(2-cyclopentylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,

7-chloro-4-{[2-(1-cyclopentenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3 -g]quinolin-3-ol,

7-chloro-2,2,9-trimethyl-4-[(5-methylhexan-2-yl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]q uinolin-3-ol,

7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,

7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyran o[2,3-g]quinolin-3-ol,

7-chloro-2,2,9-trimethyl-4-[{2-(4-thianyl)ethyl}amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,

7-chloro-4-({[6-(4-chlorophenyl)-3-pyridinyl]methyl}amino)-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,

4-[(2-benzofurylmethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]q uinolin-3-ol,

7-chloro-4-[(2-hydroxypentyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,

2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol, 4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,

4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxali n-3-ol,

4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxa lin-3-ol,

2,2-dimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol,

2,2,7,8-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3 -ol,

- 7,8-diethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinox alin-3-ol,
- 2,2,8-trimethyl-7-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinox alin-3-ol,
- 2,2,7-trimethyl-8-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinox alin-3-ol,
- 2,2,8-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol, 4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol, 3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]benzi midazol-7-one,
- 7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-a nthracen-3-on.
- 7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracen-3-on,
- 6,6-dimethyl-8-[(2-phenylethyl)amino]-2,3,4,6,7,8-hexahydro-1,5-dioxa-4-aza-anthrac en-7-ol,
- 7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-dioxa-1-aza-a nthracen-2-on,
- 6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza-anthrac en-7-ol,
- 9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]q uinolin-3-ol,
- 2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-3,7-dio l,
- 7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]q uinolin-3-ol,
- 7-chloro-2,2,9-trimethyl- $6\lambda 5$ -oxy-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol,
- $\label{eq:continuous} 7-chloro-4-\{[2-(4-fluorophenyl)ethyl]amino\}-2,2,9-trimethyl-6\lambda 5-oxy-3,4-dihydro-2\textit{H-pyr} ano[2,3-g]quinolin-3-ol,$
- 7-chloro-2,2,9-trimethyl- $6\lambda 5$ -oxy-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol,
- $4-\{[2-(4-fluorophenyl)ethyl]amino\}-7-hydroxymethyl-2,2,9-trimethyl-3,4-dihydro-2\textit{H-pyr}\}$

- ano[2,3-g]quinolin-3-ol or
- 2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol;
- (53) A benzopyran derivative or pharmaceutically acceptable salt thereof which is
- 2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol,
- 3, 3-dimethyl-1-[(2-phenylethyl)amino]-2, 3-dihydro-1 H-pyrano [3,2-f] quino lin-2-ol,
- 7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol,
- 7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-4-{[2-(4-chlorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 3-hydroxy-2,2,9-trimethyl-4-[2-(phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinol ine-7-carboxylic acid,
- 4-{[2-(4-aminophenyl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- $\label{eq:continuous} 7-chloro-4-[(2-hydroxy-2-phenylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2\emph{H-}pyrano[2,3-g]quinolin-3-ol,$
- 7-chloro-2,2,9-trimethy $[-4-{[2-(1-piperidinyl)ethyl]amino}-3,4-dihydro-2\emph{H-pyrano}[2,3-g] quinolin-3-ol,$
- 7-chloro-4-{[2-(4-chloropyrazol-1-yl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyran o[2,3-g]quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(2-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol.
- 7-chloro-2,2,9-trimethyl-4-{[2-(3-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-{[2-(4-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,
- 7-chloro-4-isopentylamino-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol, 7-chloro-4-[(2-cyclopentylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- $7-chloro-4-\{[2-(1-cyclopentenyl)ethyl]amino\}-2,2,9-trimethyl-3,4-dihydro-2\textit{H-pyrano}[2,3,4-dihydro-2,4$

- -g]quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]qui nolin-3-ol,
- 7-chloro-4-[(2-hydroxypentyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quin olin-3-ol,
- 2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol,
- 4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxali n-3-ol,
- 4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxali n-3-ol,
- 4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxa lin-3-ol,
- 2,2-dimethyl-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol,
- 4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol,
- 7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-a nthracen-3-on,
- 7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracen-3-one.
- 7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-7,8-dihydro-1*H*,6*H*-4,5-dioxa-1-aza-a nthracen-2-one,
- 9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]q uinolin-3-ol.
- 2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-3,7-dio l,
- 7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]q uinolin-3-ol,
- 7-chloro-2,2,9-trimethyl- $6\lambda 5$ -oxy-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol,
- 7-chloro-4- $\{[2-(4-fluorophenyl)ethyl]amino\}-2,2,9-trimethyl-6<math>\lambda$ 5-oxy-3,4-dihydro-2H-pyr ano[2,3-g]quinolin-3-ol,
- 7-chloro-2,2,9-trimethyl- $6\lambda 5$ -oxy-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol.
- 4-{[2-(4-fluorophenyl)ethyl]amino}-7-hydroxymethyl-2,2,9-trimethyl-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol or

2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol;

- (54) A pharmaceutical characterized by comprising the benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in any one of (1) to (53) as an active ingredient; and
- (55) A pharmaceutical for treating arrhythmia characterized by comprising the benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in any one of (1) to (53) as an active ingredient.

The compound according to the present invention has a strong prolongation effect on the refractory period and it can be used as a drug for treating arrhythmia.

Best Mode for carrying out the Invention

Respective substituents of compounds (I) or (II) according to the present invention are concretely defined below.

In the meanwhile, "n" means normal, "i" means iso, "s" means secondary, "t" means tertiary, "c" means cyclo, "o" means ortho, "m" means meta, "p" means para, "Ph" means phenyl, "Py" means pyridyl, "Bn" means benzyl, "Me" means methyl, "Et" means ethyl, "Pr" means propyl, "Bu" means butyl, "Pen" means pentyl, "Hex" means hexyl, "Ac" means acetyl, "Boc" means tertiary butoxycarbonyl and "MOM" means methoxymethyl in this specification.

Examples of C_{2-4} alkyl group are such as ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl and the like.

Examples of C_{1-4} alkyl group are such as methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl and the like.

Examples of C₁₋₆ alkyl group are such as methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, 1-pentyl, 2-pentyl, 3-pentyl, i-pentyl, neopentyl, 2,2-dimethylpropyl, 1-hexyl, 2-hexyl, 3-hexyl, 1-methyl-n-pentyl,

1,1,2-trimethyl-n-propyl, 1,2,2-trimethyl-n-propyl, 3,3-dimethyl-n-butyl and the like.

Preferably, methyl, ethyl, n-propyl, i-propyl, n-butyl, n-pentyl and i-pentyl may be mentioned.

Examples of C₃₋₈ cycloalkyl group are such as c-propyl, c-butyl, 1-methyl-c-propyl, 2-methyl-c-propyl, c-pentyl, 1-methyl-c-butyl, 2-methyl-c-butyl, 3-methyl-c-butyl, 1,2-dimethyl-c-propyl, 2,3-dimethyl-c-propyl, 1-ethyl-c-propyl, 2-ethyl-c-propyl, c-hexyl, c-hexyl, c-octyl, 1-methyl-c-hexyl, 2-methyl-c-hexyl, 3-methyl-c-propyl, 1-ethyl-c-propyl, 1-methyl-c-pentyl, 2-methyl-c-pentyl, 2-methyl-c-butyl, 2-ethyl-c-butyl, 2-ethyl

3-ethyl-c-butyl, 1,2-dimethyl-c-butyl, 1,3-dimethyl-c-butyl, 2,2-dimethyl-c-butyl, 2,3-dimethyl-c-butyl, 3,3-dimethyl-c-butyl, 1-n-propyl-c-propyl, 2-n-propyl-c-propyl, 1-i-propyl-c-propyl, 2-i-propyl-c-propyl, 1,2,2-trimethyl-c-propyl, 1,2,3-trimethyl-c-propyl, 2,2,3-trimethyl-c-propyl, 1-ethyl-2-methyl-c-propyl, 2-ethyl-1-methyl-c-propyl, 2-ethyl-2-methyl-c-propyl, and the like.

Preferably, c-pentyl and c-hexyl may be mentioned.

Examples of C₃₋₈ cycloalkenyl group are such as 1-c-pentenyl, 2-c-pentenyl, 3-c-pentenyl, 1-methyl-2-c-pentenyl, 1-methyl-3-c-pentenyl, 2-methyl-1-c-pentenyl, 2-methyl-2-c-pentenyl, 2-methyl-4-c-pentenyl, 2-methyl-5-c-pentenyl, 2-methyl-1-c-pentenyl, 3-methyl-1-c-pentenyl, 3-methyl-2-c-pentenyl, 3-methyl-3-c-pentenyl, 3-methyl-4-c-pentenyl, 3-methyl-5-c-pentenyl, 3-methyl-6-c-pentenyl, 1-c-pentenyl, 1-c-pentenyl, 1-c-pentenyl, 1-c-pentenyl, 3-c-pentenyl, 3-c-pentenyl, 1-c-pentenyl, 1-c

Preferably, 1-c-pentenyl, 2-c-pentenyl, 3-c-pentenyl, 1-c-hexenyl 2-c-hexenyl and 3-c-hexenyl may be mentioned.

Examples of halogen atom are fluorine atom, chlorine atom, bromine atom and iodine atom. Preferably, fluorine atom, chlorine atom and bromine atom may be mentioned.

Examples of C_{1-6} alkoxy group are such as methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, i-butoxy, s-butoxy, t-butoxy, 1-pentyloxy, 2-pentyloxy, 3-pentyloxy, i-pentyloxy, neopentyloxy, 2, 2-dimethylpropoxy, 1-hexyloxy, 2-hexyloxy, 3-hexyloxy, 1-methyl-n-pentyloxy, 1, 1, 2-trimethyl-n-propoxy, 1, 2, 2-trimethyl-n-propoxy, 3, 3-dimethyl-n-butoxy and the like.

Preferably, methoxy, ethoxy, n-propoxy and i-propoxy may be mentioned.

Examples of C₁₋₆ thioalkoxy group are such as methylthio, ethylthio, n-propylthio, i-propylthio, c-propylthio, n-butylthio, i-butylthio, s-butylthio, t-butylthio, n-pentylthio, i-pentylthio, neopentylthi, t-pentylthio, n-hexylthio, c-hexylthio and the like.

Examples of C₁₋₆ alkylcarbonyloxy group are such as methylcarbonyloxy, ethylcarbonyloxy, n-propylcarbonyloxy, i-propylcarbonyloxy, n-butylcarbonyloxy, i-butylcarbonyloxy, s-butylcarbonyloxy, t-butylcarbonyloxy, 1-pentylcarbonyloxy, 2-pentylcarbonyloxy, 3-pentylcarbonyloxy, t-pentylcarbonyloxy, 1-hexylcarbonyloxy, 2-hexylcarbonyloxy, 3-hexylcarbonyloxy,

1-methyl-n-pentylcarbonyloxy, 1,1,2-trimethyl-n-propylcarbonyloxy,

1,2,2-trimethyl-n-propylcarbonyloxy, 3, 3-dimethyl-n-butylcarbonyloxy and the like.

Preferably, methylcarbonyloxy, ethylcarbonyloxy, n-propylcarbonyloxy, i-propylcarbonyloxy, n-butylcarbonyloxy and t-butylcarbonyloxy may be mentioned.

Examples of C_{6-14} aryl group are such as phenyl, o-biphenylyl, m-biphenylyl, p-biphenylyl, α -naphthyl, β -naphthyl, 1-anthryl, 2-anthryl, 9-anthryl, 1-phenanthryl, 2-phenanthryl, 3-phenanthryl, 4-phenanthryl, 9-phenanthryl and the like.

Preferably, phenyl, o-biphenylyl, m-biphenylyl, p-biphenylyl, α -naphthyl and β -naphthyl may be mentioned.

 C_{2-9} heteroaryl group includes C_{2-6} single-ring heterocyclic group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a combination.

Examples of the C₂₋₆ single-ring heterocyclic group with 5- to 7-member ring are such as 2-thienyl group, 3-thienyl group, 2-furyl group, 3-furyl group, 2-pyranyl group, 3-pyranyl group, 4-pyranyl group, 1-pyrrolyl group, 2-pyrrolyl group, 3-pyrrolyl group, 1-imidazolyl group, 2-imidazolyl group, 4-imidazolyl group, 1-pyrazolyl group, 3-pyrazolyl group, 4-pyrazolyl group, 2-thiazolyl group, 4-thiazolyl group, 5-thiazolyl group, 3-isothiazolyl group, 4-isothiazolyl group, 5-isothiazolyl group, 2-oxazolyl group, 4-oxazolyl group, 5-oxazolyl group, 3-isoxazolyl group, 4-pyridyl group, 2-pyradinyl group, 5-isoxazolyl group, 2-pyradinyl group, 2-pyrimidinyl group, 4-pyrimidinyl group, 3-pyrimidinyl group, 3-pyridazinyl group, 4-pyridazinyl group, 2-1,3,4-oxadiazolyl group, 2-1,3,4-thiadiazolyl group, 3-1,2,4-thiadiazolyl group, 3-1,2,4-thiadiazolyl group, 3-1,2,5-thiadiazolyl group and the like.

Examples of the C₅₋₉ fused double-ring heterocyclic group with member atom number of 8 to 10 are 2-benzofuranyl group, 3-benzofuranyl group, 4-benzofuranyl group, 5-benzofuranyl group, 6-benzofuranyl group, 7-benzofuranyl group, 1-isobenzofuranyl group, 4-isobenzofuranyl group, 5-isobenzofuranyl group, 2-benzothienyl group, 3-benzothienyl group, 4-benzothienyl group, 5-benzothienyl group, 6-benzothienyl group, 7-benzothienyl group, 1-isobenzothienyl group, 4-isobenzothienyl group, 5-isobenzothienyl group, 2-chromenyl group, 3-chromenyl group, 4-chromenyl group, 5-chromenyl group, 6-chromenyl group, 7-chromenyl group, 8-chromenyl group, 1-indolizinyl group, 2-indolizinyl group, 3-indolizinyl group,

5-indolizinyl group, 6-indolizinyl group, 7-indolizinyl group, 8-indolizinyl group, 1-isoindolyl group, 2-isoindolyl group, 4-isoindolyl group, 5-isoindolyl group, 1-indolyl group, 2-indolyl group, 3-indolyl group, 4-indolyl group, 5-indolyl group, 6-indolyl group, 7-indolyl group, 1-indazolyl group, 2-indazolyl group, 3-indazolyl group, 4-indazolyl group, 5-indazolyl group, 6-indazolyl group, 7-indazolyl group, 1-purinyl group, 2-purinyl group, 3-purinyl group, 6-purinyl group, 7-purinyl group, 8-purinyl group, 2-quinolyl group, 3-quinolyl group, 4-quinolyl group, 5-quinolyl group, 6-quinolyl group, 7-auinolyl group, 8-guinolyl group, 1-isoguinolyl group, 3-isoguinolyl group, 4-isoquinolyl group, 5-isoquinolyl group, 6-isoquinolyl group, 7-isoquinolyl group, 8-isoquinolyl group, 1-phthalazinyl group, 5-phthalazinyl group, 6-phthalazinyl group, 1-2,7-naphthyridinyl group, 3-2,7-naphthyridinyl group, 4-2,7-naphthyridinyl group, 1-2,6-naphthyridinyl group, 3-2,6-naphthyridinyl group, 4-2,6-naphthyridinyl group, 2-1.8-naphthyridinyl group, 3-1.8-naphthyridinyl group, 4-1,8-naphthyridinyl group, 2-1.7-naphthyridinyl group, 3-1,7-naphthyridinyl group, 4-1,7-naphthyridinyl group, 5-1,7-naphthyridinyl group, 6-1,7-naphthyridinyl group, 8-1,7-naphthyridinyl group, 2-1,6-naphthyridinyl group, 3-1,6-naphthyridinyl group, 4-1,6-naphthyridinyl group, 5-1,6-naphthyridinyl group, 7-1,6-naphthyridinyl group, 8-1,6-naphthyridinyl group, 2-1.5-naphthyridinyl group, 3-1.5-naphthyridinyl group, 4-1,5-naphthyridinyl group, 6-1.5-naphthyridinyl group, 7-1,5-naphthyridinyl group, 8-1,5-naphthyridinyl group, 2-quinoxalinyl group, 5-quinoxalinyl group, 6-quinoxalinyl group, 2-quinazolinyl group, 4-quinazolinyl group, 5-quinazolinyl group, 6-quinazolinyl group, 7-quinazolinyl group, 8-quinazolinyl group, 3-cinnolinyl group, 4-cinnolinyl group, 5-cinnolinyl group, 6-cinnolinyl group, 7-cinnolinyl group, 8-cinnolinyl group, 2-pteridinyl group, 4-pteridinyl group, 6-pteridinyl group, 7-pteridinyl group, and the like.

Preferably, 2-pyridyl group, 3-pyridyl group and 4-pyridyl group may be mentioned.

 C_{2-9} heterocyclyl group includes single-ring or fused double-ring heterocyclic group composed of 1 or more atoms freely selected from nitrogen atom, oxygen atom and sulfur atom and 2 to 9 carbon atoms, and concretely includes the following groups:

Examples of C₁₋₆ alkylamino group are such as methylamino, ethylamino, n-propylamino, i-propylamino, c-propylamino, n-butylamino, i-butylamino, s-butylamino, t-butylamino, c-butylamino, 1-pentylamino, 2-pentylamino, 3-pentylamino, i-pentylamino, neopentylamino, t-pentylamino, c-pentylamino, 1-hexylamino, 2-hexylamino, 3-hexylamino, c-hexylamino, 1-methyl-n-pentylamino, 1,1,2-trimethyl-n-propylamino, 1,2,2-trimethyl-n-propylamino, 3,3-dimethyl-n-butylamino and the like.

Preferably, methylamino, ethylamino, n-propylamino, i-propylamino and n-butylamino may be mentioned.

Examples of di-C₁₋₆ alkylamino group are such as dimethylamino, diethylamino, di-n-propylamino, di-i-propylamino, di-c-propylamino, di-n-butylamino, di-i-butylamino, di-s-butylamino, di-i-butylamino, di-c-butylamino, di-1-pentylamino, di-2-pentylamino, di-3-pentylamino, di-i-pentylamino, di-neopentylamino, di-2-pentylamino, di-c-pentylamino, di-1-pentylamino, di-2-hexylamino, di-3-hexylamino, di-c-hexylamino, di-(1-methyl-n-pentyl)amino, di-(1,1,2-trimethyl-n-propyl)amino, di-(1,2,2-trimethyl-n-propyl)amino, di-(3,3-dimethyl-n-butyl)amino, methyl(ethyl)amino, methyl(n-propyl)amino, methyl(i-propyl)amino, methyl(c-propyl)amino, methyl(i-butyl)amino, methyl(s-butyl)amino, ethyl(i-butyl)amino, ethyl(i-butyl)amino, ethyl(i-butyl)amino, ethyl(s-butyl)amino, ethyl(s-butyl)amino, ethyl(s-butyl)amino, n-propyl(i-butyl)amino, n-propyl(i-butyl)amino, n-propyl(i-butyl)amino, n-propyl(s-butyl)amino, n-propyl(s-butyl)amino,

i-propyl(c-propyl)amino, i-propyl(n-butyl)amino, i-propyl(i-butyl)amino, i-propyl(s-butyl)amino, i-propyl(t-butyl)amino, i-propyl(c-butyl)amino, c-propyl(n-butyl)amino, c-propyl(i-butyl)amino, c-propyl(s-butyl)amino, c-propyl(c-butyl)amino, n-butyl(i-butyl)amino, n-butyl(s-butyl)amino, n-butyl(c-butyl)amino, i-butyl(c-butyl)amino, i-butyl(c-butyl)amino, s-butyl(t-butyl)amino, s-butyl(c-butyl)amino, t-butyl(c-butyl)amino and the like.

Preferably, dimethylamino, diethylamino, di-n-propylamino, di-i-propylamino and di-n-butylamino may be mentioned.

Examples of C₁₋₆ alkylcarbonylamino group are such as methylcarbonylamino, ethylcarbonylamino, n-propylcarbonylamino, i-propylcarbonylamino, n-butylcarbonylamino, i-butylcarbonylamino, s-butylcarbonylamino, t-butylcarbonylamino, 1-pentylcarbonylamino, 2-pentylcarbonylamino, 3-penylcarbonylamino, i-pentylcarbonylamino, neopentylcarbonylamino, t-pentylcarbonylamino, 1-hexylcarbonylamino, 2-hexylcarbonylamino, 3-hexylcarbonylamino and the like.

Preferably, methylcarbonylamino, ethylcarbonylamino, n-propylcarbonylamino, i-propylcarbonylamino and n-butylcarbonylamino may be mentioned.

Examples of C₁₋₆ alkylsulfonylamino group are such as methylsulfonylamino, ethylsulfonylamino, n-propylsulfonylamino, i-propylsulfonylamino, n-butylsulfonylamino, i-butylsulfonylamino, t-butylsulfonylamino, t-butylsulfonylamino, 1-pentylsulfonylamino, 2-pentylsulfonylamino, 3-pentylsulfonylamino, i-pentylsulfonylamino, neopentylsulfonylamino, t-pentylsulfonylamino, 1-hexylsulfonylamino, 2-hexylsulfonylamino, 3-hexylsulfonylamino and the like.

Preferably, methylsulfonylamino, ethylsulfonylamino, n-propylsulfonylamino, i-propylsulfonylamino and n-butylsulfonylamino may be mentioned.

Examples of C₁₋₆ alkylaminocarbonyl group are such as methylaminocarbonyl, ethylaminocarbonyl, n-propylaminocarbonyl, i-propyl-aminocarbonyl, n-butylaminocarbonyl, i-butylaminocarbonyl, s-butylaminocarbonyl, t-butylaminocarbonyl, 1-pentylaminocarbonyl, 2-pentylaminocarbonyl, 3-pentyl-aminocarbonyl, i-pentylaminocarbonyl, neopentylaminocarbonyl, t-pentylamino-carbonyl, 1-hexylaminocarbonyl, 2-hexylaminocarbonyl, 3-hexylaminocarbonyl and the like.

Preferably, methylaminocarbonyl, ethylaminocarbonyl, n-propylaminocarbonyl, i-propylaminocarbonyl and n-butylaminocarbonyl may be mentioned.

Examples of di-C₁₋₆ alkylaminocarbonyl group are such as dimethylaminocarbonyl, diethylaminocarbonyl, di-n-propylaminocarbonyl, di-i-propylaminocarbonyl, di-c-propylaminocarbonyl, di-n-butylaminocarbonyl, di-i-butylaminocarbonyl, di-s-butylaminocarbonyl, di-t-butylaminocarbonyl, di-c-butylaminocarbonyl, di-1-pentylaminocarbonyl, di-2-pentylaminocarbonyl, di-3-pentylaminocarbonyl, di-i-pentylaminocarbonyl, di-neopentylaminocarbonyl, di-t-pentylaminocarbonyl, di-c-pentylaminocarbonyl, di-1-hexylaminocarbonyl, di-2-hexylaminocarbonyl, di-3-hexylaminocarbonyl, di-c-hexylaminocarbonyl, di-(1-methyl-n-pentyl)aminocarbonyl, di-(1,1,2-trimethyl-n-propyl)aminocarbonyl, di-(1,2,2-trimethyl-n-propyl)aminocarbonyl, di-(3,3-dimethyl-n-butyl)aminocarbonyl, methyl(ethyl)aminocarbonyl, methyl(n-propyl)aminocarbonyl, methyl(i-propyl)aminocarbonyl, methyl(c-propyl)aminocarbonyl, methyl(n-butyl)aminocarbonyl, methyl(i-butyl)aminocarbonyl, methyl(s-butyl)aminocarbonyl, methyl(t-butyl)aminocarbonyl, methyl(c-butyl)aminocarbonyl, ethyl(n-propyl)aminocarbonyl, ethyl(i-propyl)aminocarbonyl, ethyl(c-propyl)aminocarbonyl, ethyl(n-butyl)aminocarbonyl, ethyl(i-butyl)aminocarbonyl, ethyl(s-butyl)aminocarbonyl, ethyl(t-butyl)aminocarbonyl, ethyl(c-butyl)aminocarbonyl, n-propyl(i-propyl)aminocarbonyl, n-propyl(c-propyl)aminocarbonyl, n-propyl(n-butyl)aminocarbonyl, n-propyl(i-butyl)aminocarbonyl, npropyl(s-butyl)aminocarbonyl, n-propyl(t-butyl)aminocarbonyl, n-propyl(c-butyl)aminocarbonyl, i-propyl(c-butyl)aminocarbonyl, i-propyl(n-butyl)aminocarbonyl, i-propyl(i-butyl)aminocarbonyl, i-propyl(s-butyl)aminocarbonyl, i-propyl(t-butyl)aminocarbonyl, i-propyl(c-butyl)aminocarbonyl, c-propyl(n-butyl)aminocarbonyl, c-propyl(i-butyl)aminocarbonyl, c-propyl(s-butyl)aminocarbonyl, c-propyl(t-butyl)aminocarbonyl, c-propyl(c-butyl)aminocarbonyl, n-butyl(i-butyl)aminocarbonyl, n-butyl(s-butyl)aminocarbonyl, n-butyl(t-butyl)aminocarbonyl, n-butyl(c-butyl)aminocarbonyl, i-butyl(s-butyl)aminocarbonyl, i-butyl(t-butyl)aminocarbonyl, i-butyl(t-butyl)aminocarbonyl, i-butyl(c-butyl)aminocarbonyl, s-butyl(t-butyl)aminocarbonyl, s-butyl(c-butyl)aminocarbonyl, t-butyl(c-butyl)aminocarbonyl, and the like.

Preferably, dimethylaminocarbonyl, diethylaminocarbonyl, di-n-propylaminocarbonyl, di-i-propylaminocarbonyl, di-c-propylaminocarbonyl and

di-n-butylaminocarbonyl may be mentioned.

Examples of C_{1-6} alkylcarbonyl group are such as methylcarbonyl, ethylcarbonyl, n-propylcarbonyl, i-propylcarbonyl, n-butylcarbonyl, i-butylcarbonyl, s-butylcarbonyl, t-butylcarbonyl, 1-pentylcarbonyl, 2-pentylcarbonyl, 3-pentylcarbonyl, i-pentylcarbonyl, neopentylcarbonyl, t-pentylcarbonyl, 1-hexylcarbonyl, 2-hexylcarbonyl, 3-hexylcarbonyl and the like.

Preferably, methylcarbonyl, ethylcarbonyl, n-propylcarbonyl, i-propylcarbonyl and n-butylcarbonyl may be mentioned.

Examples of C₃₋₈ cycloalkylcarbonyl group are such as c-propylcarbonyl, c-butylcarbonyl, 1-methyl-c-propylcarbonyl, 2-methyl-c-propylcarbonyl, c-pentylcarbonyl, 1-methyl-c-butylcarbonyl, 2-methyl-c-butylcarbonyl, 3-methyl-c-butylcarbonyl, 1,2-dimethyl-c-propylcarbonyl,

- 2,3-dimethyl-c-propylcarbonyl, 1-ethyl-c-propylcarbonyl, 2-ethyl-c-propylcarbonyl,
- c-hexylcarbonyl, c-heptylcarbonyl, c-octylcarbonyl, 1-methyl-c-hexylcarbonyl,
- 2-methyl-c-hexylcarbonyl, 3-methyl-c-hexylcarbonyl, 1,2-dimehtyl-c-hexylcarbonyl,
- 2,3-dimethyl-c-propylcarbonyl, 1-ethyl-c-propylcarbonyl, 1-methyl-c-pentylcarbonyl,
- 2-methyl-c-pentylcarbonyl, 3-methyl-c-pentylcarbonyl, 1-ethyl-c-butylcarbonyl,
- 2-ethyl-c-butylcarbonyl, 3-ethyl-c-butylcarbonyl, 1,2-dimethyl-c-butylcarbonyl,
- 1,3-dimethyl-c-butylcarbonyl, 2,2-dimethyl-c-butylcarbonyl,
- 2,3-dimethyl-c-butylcarbonyl, 2,4-dimethyl-c-butylcarbonyl,
- 3,3-dimethyl-c-butylcarbonyl, 1-n-propyl-c-propylcarbonyl, 2-n-propyl-c-propylcarbonyl, 1-i-propyl-c-propylcarbonyl, 2-i-propyl-c-propylcarbonyl,
- 1,2,2-trimethyl-c-propylcarbonyl, 1,2,3-trimethyl-c-propylcarbonyl,
- 2,2,3-trimethyl-c-propylcarbonyl, 1-ethyl-2-methyl-c-propylcarbonyl,
- 2-ethyl-1-methyl-c-propylcarbonyl, 2-ethyl-2-methyl-c-propylcarbonyl,
- 2-ethyl-3-methyl-c-propylcarbonyl, and the like.

Preferably, c-pentylcarbonyl and c-hexylcarbonyl may be mentioned.

Examples of C_{1-6} alkoxycarbonyl group are such as methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, i-propoxycarbonyl, n-butoxycarbonyl, i-butoxycarbonyl, s-butoxycarbonyl, t-butoxycarbonyl, 1-pentyloxycarbonyl, 2-pentyloxycarbonyl, 3-pentyloxycarbonyl, i-pentyloxycarbonyl, neopentyloxycarbonyl, t-pentyloxycarbonyl, 1-hexyloxycarbonyl, 2-hexyloxycarbonyl, 3-hexyloxycarbonyl and the like.

Preferably, methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, i-propoxycarbonyl, n-butoxycarbonyl, i-butoxycarbonyl, s-butoxycarbonyl and

t-butoxycarbonyl may be mentioned.

Examples of C_{1-6} alkylsulfonyl group are such as methanesulfonyl, trifluoromethanesulfonyl, ethanesulfonyl and the like.

Examples of C_{6-14} arylcarbonyl group are such as benzoyl, o-biphenylylcarbonyl, m-biphenylylcarbonyl, p-biphenylylcarbonyl, α -naphthylcarbonyl, β -naphthylcarbonyl, 1-anthrylcarbonyl, 2-anthrylcarbonyl, 9-anthrylcarbonyl, 1-phenanthrylcarbonyl, 2-phenanthrylcarbonyl, 3-phenanthrylcarbonyl, 4-phenanthrylcarbonyl, 9-phenanthrylcarbonyl and the like.

Preferably, benzoyl, o-biphenylylcarbonyl, m-biphenylylcarbonyl, p-biphenylylcarbonyl, α -naphthylcarbonyl and β -naphthylcarbonyl may be mentioned.

 C_{2-9} heteroarylcarbonyl group includes C_{2-6} single-ring heterocyclic carbonyl group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic carbonyl group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a combination.

Examples of the C₂₋₆ single-ring heterocyclic carbonyl group with 5- to 7-member ring are such as 2-thienylcarbonyl group, 3-thienylcarbonyl group, 2-furylcarbonyl group, 3-furylcarbonyl group, 2-pyranylcarbonyl group, 3-pyranylcarbonyl group, 4-pyranylcarbonyl group, 1-pyrrolylcarbonyl group, 2-pyrrolylcarbonyl group, 3-pyrrolylcarbonyl group, 1-imidazolylcarbonyl group. 2-imidazolylcarbonyl group, 4-imidazolylcarbonyl group, 1-pyrazolylcarbonyl group, 3-pyrazolylcarbonyl group, 4-pyrazolylcarbonyl group, 2-thiazolylcarbonyl group, 4-thiazolylcarbonyl group, 5-thiazolylcarbonyl group, 3-isothiazolylcarbonyl group, 4-isothiazolylcarbonyl group, 5-isothiazolylcarbonyl group, 2-oxazolylcarbonyl group, 4-oxazolylcarbonyl group, 5-oxazolylcarbonyl group, 3-isoxazolylcarbonyl group, 4-isoxazolylcarbonyl group, 5-isoxazolylcarbonyl group, 2-pyridylcarbonyl group, 3-pyridylcarbonyl group, 4-pyridylcarbonyl group, 2-pyradinylcarbonyl group, 2-pyrimidinylcarbonyl group, 4-pyrimidinylcarbonyl group, 5-pyrimidinylcarbonyl group, 3-pyridazinylcarbonyl group, 4-pyridazinylcarbonyl group, 2-1,3,4-oxadiazolylcarbonyl group, 2-1,3,4-thiadiazolylcarbonyl group, 3-1,2,4-oxadiazolylcarbonyl group, 5-1,2,4-oxadiazolylcarbonyl group, 3-1,2,4-thiadiazolylcarbonyl group. 5-1,2,4-thiadiazolylcarbonyl group, 3-1,2,5-oxadiazolylcarbonyl group, 3-1,2,5-thiadiazolylcarbonyl group and the like.

Examples of the C_{5-9} fused double-ring heterocyclic carbonyl group with member atom number of 8 to 10 are 2-benzofuranylcarbonyl group,

3-benzofuranylcarbonyl group, 4-benzofuranylcarbonyl group, 5-benzofuranylcarbonyl group, 6-benzofuranylcarbonyl group, 7-benzofuranylcarbonyl group, 1-isobenzofuranylcarbonyl group, 4-isobenzofuranylcarbonyl group, 5-isobenzofuranylcarbonyl group, 2-benzothienylcarbonyl group, 3-benzothienylcarbonyl group, 4-benzothienylcarbonyl group, 5-benzothienylcarbonyl group, 6-benzothienylcarbonyl group, 7-benzothienylcarbonyl group, 1-isobenzothienylcarbonyl group, 4-isobenzothienylcarbonyl group, 5-isobenzothienylcarbonyl group, 2-chromenylcarbonyl group, 3-chromenylcarbonyl group, 4-chromenylcarbonyl group, 5-chromenylcarbonyl group, 6-chromenylcarbonyl group, 7-chromenylcarbonyl group, 8-chromenylcarbonyl group, 1-indolizinylcarbonyl group, 2-indolizinylcarbonyl group, 3-indolizinylcarbonyl group, 5-indolizinylcarbonyl group, 6-indolizinylcarbonyl group, 7-indolizinylcarbonyl group, 8-indolizinylcarbonyl group, 1-isoindolylcarbonyl group, 2-isoindolylcarbonyl group, 4-isoindolylcarbonyl group, 5-isoindolylcarbonyl group, 1-indolylcarbonyl group, 2-indolylcarbonyl group, 3-indolylcarbonyl group, 4-indolylcarbonyl group, 5-indolylcarbonyl group, 6-indolylcarbonyl group, 7-indolylcarbonyl group, 1-indazolylcarbonyl group, 2-indazolylcarbonyl group, 3-indazolylcarbonyl group, 4-indazolylcarbonyl group, 5-indazolylcarbonyl group, 6-indazolylcarbonyl group, 7-indazolylcarbonyl group, 1-purinylcarbonyl group, 2-purinylcarbonyl group, 3-purinylcarbonyl group, 6-purinylcarbonyl group, 7-purinylcarbonyl group, 8-purinylcarbonyl group, 2-quinolylcarbonyl group, 3-quinolylcarbonyl group, 4-quinolylcarbonyl group, 5-quinolylcarbonyl group, 6-quinolylcarbonyl group, 7-quinolylcarbonyl group, 8-quinolylcarbonyl group, 1-isoquinolylcarbonyl group, 3-isoquinolylcarbonyl group, 4-isoquinolylcarbonyl group, 5-isoquinolylcarbonyl group, 6-isoquinolylcarbonyl group, 7-isoquinolylcarbonyl group, 8-isoquinolylcarbonyl group, 1-phthalazinylcarbonyl group, 5-phthalazinylcarbonyl group, 6-phthalazinylcarbonyl group, 1-2,7-naphthyridinylcarbonyl group, 3-2,7-naphthyridinylcarbonyl group, 4-2,7-naphthyridinylcarbonyl group, 1-2,6-naphthyridinylcarbonyl group, 3-2,6-naphthyridinylcarbonyl group, 4-2,6-naphthyridinylcarbonyl group, 2-1,8-naphthyridinylcarbonyl group, 3-1,8-naphthyridinylcarbonyl group, 4-1,8-naphthyridinylcarbonyl group, 2-1,7-naphthyridinylcarbonyl group, 3-1,7-naphthyridinylcarbonyl group, 4-1,7-naphthyridinylcarbonyl group, 5-1,7-naphthyridinylcarbonyl group, 6-1,7-naphthyridinylcarbonyl group, 8-1,7-naphthyridinylcarbonyl group, 2-1,6-naphthyridinylcarbonyl group, 3-1,6-naphthyridinylcarbonyl group, 4-1,6-naphthyridinylcarbonyl group,

5-1,6-naphthyridinylcarbonyl group, 7-1,6-naphthyridinylcarbonyl group,

8-1,6-naphthyridinylcarbonyl group, 2-1,5-naphthyridinylcarbonyl group,

3-1,5-naphthyridinylcarbonyl group, 4-1,5-naphthyridinylcarbonyl group,

6-1,5-naphthyridinylcarbonyl group, 7-1,5-naphthyridinylcarbonyl group,

8-1,5-naphthyridinylcarbonyl group, 2-quinoxalinylcarbonyl group,

5-quinoxalinylcarbonyl group, 6-quinoxalinylcarbonyl group, 2-quinazolinylcarbonyl group, 4-quinazolinylcarbonyl group, 5-quinazolinylcarbonyl group,

6-quinazolinylcarbonyl group, 7-quinazolinylcarbonyl group, 8-quinazolinylcarbonyl group, 3-cinnolinylcarbonyl group, 4-cinnolinylcarbonyl group, 5-cinnolinylcarbonyl group, 6-cinnolinylcarbonyl group, 7-cinnolinylcarbonyl group, 8-cinnolinylcarbonyl group, 2-pteridinylcarbonyl group, 4-pteridinylcarbonyl group, 6-pteridinylcarbonyl group, 7-pteridinylcarbonyl group, and the like.

Preferably, 2-pyridylcarbonyl group, 3-pyridylcarbonyl group and 4-pyridylcarbonyl group may be mentioned.

Examples of C_{6-14} arylsulfonyl group are such as phenylsulfonyl, o-biphenylylsulfonyl, m-biphenylylsulfonyl, p-biphenylylsulfonyl, α -naphthylsulfonyl, β -naphthylsulfonyl, 1-anthrylsulfonyl, 2-anthrylsulfonyl, 9-anthrylsulfonyl, 1-phenanthrylsulfonyl, 2-phenanthrylsulfonyl, 3-phenanthrylsulfonyl, 4-phenanthrylsulfonyl, 9-phenanthrylsulfonyl and the like.

Preferably, phenylsulfonyl, o-biphenylylsulfonyl, m-biphenylylsulfonyl, p-biphenylylsulfonyl, α -naphthylsulfonyl and β -naphthylsulfonyl may be mentioned.

 C_{2-9} heteroaryl sulfonyl group includes C_{2-6} single-ring heterocyclic sulfonyl group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic sulfonyl group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a combination.

Examples of the C₂₋₆ single-ring heterocyclic sulfonyl group with 5- to 7-member ring are such as 2-thienylsulfonyl group, 3-thienylsulfonyl group, 2-furylsulfonyl group, 3-furylsulfonyl group, 2-pyranylsulfonyl group, 3-pyranylsulfonyl group, 4-pyranylsulfonyl group, 1-pyrrolylsulfonyl group, 2-pyrrolylsulfonyl group, 3-pyrrolylsulfonyl group, 1-imidazolylsulfonyl group, 2-imidazolylsulfonyl group, 4-imidazolylsulfonyl group, 1-pyrazolylsulfonyl group, 3-pyrazolylsulfonyl group, 4-pyrazolylsulfonyl group, 2-thiazolylsulfonyl group, 4-thiazolylsulfonyl group, 5-thiazolylsulfonyl group, 2-oxazolylsulfonyl group, 4-oxazolylsulfonyl group, 5-isothiazolylsulfonyl group, 2-oxazolylsulfonyl group, 4-oxazolylsulfonyl group,

5-oxazolylsulfonyl group, 3-isoxazolylsulfonyl group, 4-isoxazolylsulfonyl group, 5-isoxazolylsulfonyl group, 2-pyridylsulfonyl group, 3-pyridylsulfonyl group, 4-pyridylsulfonyl group, 2-pyradinylsulfonyl group, 2-pyrimidinylsulfonyl group, 3-pyridazinylsulfonyl group, 4-pyridazinylsulfonyl group, 5-pyrimidinylsulfonyl group, 3-pyridazinylsulfonyl group, 2-1,3,4-oxadiazolylsulfonyl group, 2-1,3,4-thiadiazolylsulfonyl group, 3-1,2,4-oxadiazolylsulfonyl group, 5-1,2,4-oxadiazolylsulfonyl group, 3-1,2,4-thiadiazolylsulfonyl group, 3-1,2,5-oxadiazolylsulfonyl group, 3-1,2,5-thiadiazolylsulfonyl group and the like.

Examples of the C₅₋₉ fused double-ring heterocyclic sulfonyl group with member atom number of 8 to 10 are 2-benzofuranylsulfonyl group, 3-benzofuranylsulfonyl group, 4-benzofuranylsulfonyl group, 5-benzofuranylsulfonyl group, 6-benzofuranylsulfonyl group, 7-benzofuranylsulfonyl group, 1-isobenzofuranylsulfonyl group, 4-isobenzofuranylsulfonyl group. 5-isobenzofuranylsulfonyl group, 2-benzothienylsulfonyl group, 3-benzothienylsulfonyl group, 4-benzothienylsulfonyl group, 5-benzothienylsulfonyl group, 6-benzothienylsulfonyl group, 7-benzothienylsulfonyl group, 1-isobenzothienylsulfonyl group, 4-isobenzothienylsulfonyl group, 5-isobenzothienylsulfonyl group, 2-chromenylsulfonyl group, 3-chromenylsulfonyl group, 4-chromenylsulfonyl group, 5-chromenylsulfonyl group, 6-chromenylsulfonyl group, 7-chromenylsulfonyl group, 8-chromenylsulfonyl group, 1-indolizinylsulfonyl group, 2-indolizinylsulfonyl group, 3-indolizinylsulfonyl group, 5-indolizinylsulfonyl group, 6-indolizinylsulfonyl group, 7-indolizinylsulfonyl group, 8-indolizinylsulfonyl group, 1-isoindolylsulfonyl group, 2-isoindolylsulfonyl group, 4-isoindolylsulfonyl group, 5-isoindolylsulfonyl group, 1-indolylsulfonyl group, 2-indolylsulfonyl group, 3-indolylsulfonyl group, 4-indolylsulfonyl group, 5-indolylsulfonyl group, 6-indolylsulfonyl group, 7-indolylsulfonyl group, 1-indazolylsulfonyl group, 2-indazolylsulfonyl group, 3-indazolylsulfonyl group, 4-indazolylsulfonyl group, 5-indazolylsulfonyl group, 6-indazolylsulfonyl group, 7-indazolylsulfonyl group, 1-purinylsulfonyl group, 2-purinylsulfonyl group, 3-purinylsulfonyl group, 6-purinylsulfonyl group, 7-purinylsulfonyl group, 8-purinylsulfonyl group, 2-quinolylsulfonyl group, 3-quinolylsulfonyl group, 4-quinolylsulfonyl group, 5-quinolylsulfonyl group, 6-quinolylsulfonyl group, 7-quinolylsulfonyl group, 8-quinolylsulfonyl group, 1-isoquinolylsulfonyl group, 3-isoquinolylsulfonyl group, 4-isoquinolylsulfonyl group, 5-isoquinolylsulfonyl group, 6-isoquinolylsulfonyl group, 7-isoquinolylsulfonyl group,

8-isoquinolylsulfonyl group, 1-phthalazinylsulfonyl group, 5-phthalazinylsulfonyl group, 6-phthalazinylsulfonyl group, 1-2,7-naphthyridinylsulfonyl group, 2.2.7 pephthyridinylsulfonyl group.

3-2,7-naphthyridinylsulfonyl group, 4-2,7-naphthyridinylsulfonyl group,

1-2,6-naphthyridinylsulfonyl group, 3-2,6-naphthyridinylsulfonyl group,

4-2,6-naphthyridinylsulfonyl group, 2-1,8-naphthyridinylsulfonyl group,

3-1,8-naphthyridinylsulfonyl group, 4-1,8-naphthyridinylsulfonyl group,

2-1,7-naphthyridinylsulfonyl group, 3-1,7-naphthyridinylsulfonyl group,

4-1,7-naphthyridinylsulfonyl group, 5-1,7-naphthyridinylsulfonyl group,

6-1,7-naphthyridinylsulfonyl group, 8-1,7-naphthyridinylsulfonyl group,

2-1,6-naphthyridinylsulfonyl group, 3-1,6-naphthyridinylsulfonyl group,

4-1,6-naphthyridinylsulfonyl group, 5-1,6-naphthyridinylsulfonyl group,

7-1,6-naphthyridinylsulfonyl group, 8-1,6-naphthyridinylsulfonyl group,

2-1,5-naphthyridinylsulfonyl group, 3-1,5-naphthyridinylsulfonyl group,

4-1,5-naphthyridinylsulfonyl group, 6-1,5-naphthyridinylsulfonyl group,

7-1,5-naphthyridinylsulfonyl group, 8-1,5-naphthyridinylsulfonyl group,

2-quinoxalinylsulfonyl group, 5-quinoxalinylsulfonyl group, 6-quinoxalinylsulfonyl group, 2-quinazolinylsulfonyl group, 4-quinazolinylsulfonyl group,

5-quinazolinylsulfonyl group, 6-quinazolinylsulfonyl group, 7-quinazolinylsulfonyl group, 8-quinazolinylsulfonyl group, 3-cinnolinylsulfonyl group, 4-cinnolinylsulfonyl group, 5-cinnolinylsulfonyl group, 6-cinnolinylsulfonyl group, 7-cinnolinylsulfonyl group, 8-cinnolinylsulfonyl group, 2-pteridinylsulfonyl group, 4-pteridinylsulfonyl group, 6-pteridinylsulfonyl group, 7-pteridinylsulfonyl group, and the like.

Preferably, 2-pyridylsulfonyl group, 3-pyridylsulfonyl group and 4-pyridylsulfonyl group may be mentioned.

Examples of C_{6-14} arylamino group are such as phenylamino, o-biphenylylamino, m-biphenylylamino, p-biphenylylamino, α -naphthylamino, β -naphthylamino, 1-anthrylamino, 2-anthrylamino, 9-anthrylamino, 1-phenanthrylamino, 2-phenanthrylamino, 3-phenanthrylamino, 4-phenanthrylamino, 9-phenanthrylamino and the like.

Preferably, phenylamino, o-biphenylylamino, m-biphenylylamino, p-biphenylylamino, α -naphthylamino and β -naphthylamino may be mentioned.

 C_{2-9} heteroarylamino group includes C_{2-6} single-ring heterocyclic amino group with 5- to 7-member ring and C_{5-9} fused double-ring heterocyclic amino group with member atom number of 8 to 10, which may contain 1 to 3 hetero atoms selected from the group consisting of oxygen atom, nitrogen atom and sulfur atom alone or in a

combination.

Examples of the C₂₋₆ single-ring heterocyclic amino group with 5- to 7-member ring are such as 2-thienylamino group, 3-thienylamino group, 2-furylamino group, 3-furylamino group, 2-pyranylamino group, 3-pyranylamino group, 4-pyranylamino group, 1-pyrrolylamino group, 2-pyrrolylamino group, 3-pyrrolylamino group, 1-imidazolylamino group, 2-imidazolylamino group, 4-imidazolylamino group, 1-pyrazolylamino group, 3-pyrazolylamino group, 4-pyrazolylamino group, 2-thiazolylamino group, 4-thiazolylamino group, 5-thiazolylamino group, 3-isothiazolylamino group, 4-isothiazolylamino group, 5-isothiazolylamino group, 2-oxazolylamino group, 4-oxazolylamino group, 5-oxazolylamino group, 3-isoxazolylamino group, 4-isoxazolylamino group, 5-isoxazolylamino group, 2-pyridylamino group, 3-pyridylamino group, 4-pyridylamino group, 2-pyradinylamino group, 2-pyrimidinylamino group, 4-pyrimidinylamino group, 5-pyrimidinylamino group, 3-pyridazinylamino group, 4-pyridazinylamino group, 2-1,3,4-oxadiazolylamino group. 2-1,3,4-thiadiazolylamino group, 3-1,2,4-oxadiazolylamino group, 5-1,2,4-oxadiazolylamino group, 3-1,2,4-thiadiazolylamino group, 5-1,2,4-thiadiazolylamino group, 3-1,2,5-oxadiazolylamino group, 3-1,2,5-thiadiazolylamino group and the like.

Examples of the C₅₋₉ fused double-ring heterocyclic amino group with member atom number of 8 to 10 are 2-benzofuranylamino group, 3-benzofuranylamino group, 4-benzofuranylamino group, 5-benzofuranylamino group, 6-benzofuranylamino group, 7-benzofuranylamino group, 1-isobenzofuranylamino group, 4-isobenzofuranylamino group, 5-isobenzofuranylamino group, 2-benzothienylamino group, 3-benzothienylamino group, 4-benzothienylamino group. 5-benzothienylamino group, 6-benzothienylamino group, 7-benzothienylamino group, 1-isobenzothienylamino group, 4-isobenzothienylamino group, 5-isobenzothienylamino group, 2-chromenylamino group, 3-chromenylamino group, 4-chromenylamino group, 5-chromenylamino group, 6-chromenylamino group, 7-chromenylamino group, 8-chromenylamino group, 1-indolizinylamino group, 2-indolizinylamino group, 3-indolizinylamino group, 5-indolizinylamino group, 6-indolizinylamino group, 7-indolizinylamino group, 8-indolizinylamino group, 1-isoindolylamino group, 2-isoindolylamino group, 4-isoindolylamino group, 5-isoindolylamino group, 1-indolylamino group, 2-indolylamino group, 3-indolylamino group, 4-indolylamino group, 5-indolylamino group, 6-indolylamino group, 7-indolylamino group, 1-indazolylamino group, 2-indazolylamino group,

3-indazolylamino group, 4-indazolylamino group, 5-indazolylamino group,

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6-indazolylamino group, 7-indazolylamino group, 1-purinylamino group,
2-purinylamino group, 3-purinylamino group, 6-purinylamino group, 7-purinylamino
group, 8-purinylamino group, 2-quinolylamino group, 3-quinolylamino group,
4-quinolylamino group, 5-quinolylamino group, 6-quinolylamino group,
7-quinolylamino group, 8-quinolylamino group, 1-isoquinolylamino group,
3-isoquinolylamino group, 4-isoquinolylamino group, 5-isoquinolylamino group,
6-isoquinolylamino group, 7-isoquinolylamino group, 8-isoquinolylamino group,
1-phthalazinylamino group, 5-phthalazinylamino group, 6-phthalazinylamino group,
1-2,7-naphthyridinylamino group, 3-2,7-naphthyridinylamino group,
4-2,7-naphthyridinylamino group, 1-2,6-naphthyridinylamino group,
3-2,6-naphthyridinylamino group, 4-2,6-naphthyridinylamino group,
2-1,8-naphthyridinylamino group, 3-1,8-naphthyridinylamino group,
4-1,8-naphthyridinylamino group, 2-1,7-naphthyridinylamino group,
3-1,7-naphthyridinylamino group, 4-1,7-naphthyridinylamino group,
5-1,7-naphthyridinylamino group, 6-1,7-naphthyridinylamino group,
8-1,7-naphthyridinylamino group, 2-1,6-naphthyridinylamino group,
3-1,6-naphthyridinylamino group, 4-1,6-naphthyridinylamino group,
5-1,6-naphthyridinylamino group, 7-1,6-naphthyridinylamino group,
8-1,6-naphthyridinylamino group, 2-1,5-naphthyridinylamino group,
3-1,5-naphthyridinylamino group, 4-1,5-naphthyridinylamino group,
6-1,5-naphthyridinylamino group, 7-1,5-naphthyridinylamino group,
8-1,5-naphthyridinylamino group, 2-quinoxalinylamino group, 5-quinoxalinylamino
group, 6-quinoxalinylamino group, 2-quinazolinylamino group, 4-quinazolinylamino
group, 5-quinazolinylamino group, 6-quinazolinylamino group, 7-quinazolinylamino
group, 8-quinazolinylamino group, 3-cinnolinylamino group, 4-cinnolinylamino group,
5-cinnolinylamino group, 6-cinnolinylamino group, 7-cinnolinylamino group,
8-cinnolinylamino group, 2-pteridinylamino group, 4-pteridinylamino group,
6-pteridinylamino group, 7-pteridinylamino group, and the like.
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Preferably, 2-pyridylamino group, 3-pyridylamino group and 4-pyridylamino group may be mentioned.

Concrete examples of substituents on the compounds used in the present invention are as follows.

Concrete examples of R^1 and R^2 are preferably methyl. Concrete examples of R^3 are preferably hydroxy group.

Concrete examples of R⁴ are preferably hydrogen atom.

Concrete examples of R⁵ are preferably hydrogen atom.

Concrete examples of -N- $(CH_2)_m$ -V- $(CH_2)_n$ -R⁶ are preferably the following 1)

to 4).

1)

N-Me

N-Et



$$\begin{array}{c} \underbrace{\mathsf{Me}} \\ \underbrace{\mathsf{N}} \\ \underbrace{\mathsf{N}}$$

42

2)

43

Concrete examples of A are preferably the following 1) and 2).

2)

The preferable compounds used in the present invention include the followings:

- (1) A benzopyran derivative of formula (I) or (II), or pharmaceutically acceptable salt thereof, wherein both R¹ and R² are methyl, R³ is hydroxy group, and R⁴ is hydrogen atom;
- (2) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (1), which is the compound of formula (I);
- (3) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (2), wherein V is a bond, m is an integer of 1 to 3, n is 0 or 1 and R^6 is benzene ring;
- (4) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein V is CR⁷R⁸ wherein R⁷ is hydroxy group and R⁸ is hydrogen atom, and m is 0 or 1;
- (5) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein R⁶ is alkyl group, cycloalkyl group or cycloalkynyl ring;
- (6) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein V is CR⁷R⁸ wherein R⁷ is hydroxy group and R⁸ is hydrogen atom, and m is 0 or 1;
- (7) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (3), wherein A is the group of formula (VIII)

Formula (VIII)

- (8) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (4), wherein A is the group of formula (VIII);
- (9) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (5), wherein A is the group of formula (VIII);
- (10) The benzopyran derivative or pharmaceutically acceptable salt thereof as set forth in (6), wherein A is the group of formula (VIII);

Hereinafter, concrete examples of the compounds that can be used in the present invention are shown, but the present invention is not limited thereto. In the meanwhile, "Me" means methyl, "Et" means ethyl, "Pr" means propyl, "Bu" means butyl, "Ac" means acetyl (COCH₃), and "-" means a bond.

HN-R

	HN ~	HN	HN	HN
	HN	ÓH.	HN	HN N N
	HN	HN F	HN	
	HN	HN		F HN N
	LINI	HN	HN	HN
	HN	HN	HN	HN S
	HN	F	F	HN O
	HN	HN	HN COOH	HN
	HN	HNOH	HN NH ₂	HN
	HN	HN	HN	HN
		ő	HN Me	HN N CI
	HN	HN	HN	N
	HN OH	HN		HN
_	HN	HN	N OH	

	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
	Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
	Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
	Н	Н	nPr	H	SO₃H	Н	Н	Н	SO₃H
	H	Н	nBu	Н	Cl	Н	Н	Н	CI
	Н	Н	tBu	Н	Br	Н	Н	Н	Br
	Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
	Me	Æt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
	Me	iPr	Н	Me	CH ₂ NHMe	H	Me	Н	CH ₂ NHMe
	Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
	Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
	Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
	Et	Ph	Н	Et	CONH ₂	H	Et	Н	CONH ₂
	Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
	Et	Н	iPr	Εt	CONHMs	iPr	Et	iPr	CONHMs
	iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
	nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
	nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
	tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
	Ph	CI	Et '	Ph	SO₃H	Et	Ph	Et	Н
	CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
	CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
(CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	Cl
(CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
	CH ₂ NH ₂	Ph	Cl	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	Cl
	CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
	CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH_2NH_2	nPr	Н
	CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
C	CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
	_ CH₂Ph	Et,	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
	CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
С	H ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph	Н
			•						

_	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
_	Н					11	10	1	K
		Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
	Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
	Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
	Н	Н	nBu	Н	CI	Н	Н	Н	CI
	Н	Н	tBu	Н	Br	Н	Н	Н	Br
,	Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
	Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
	Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	H	CH ₂ NHMe
	Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
	Me	nBu	Н	Me	COMe	Н	Ме	Н	COMe
	Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
	Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
	Et	Н	Et	Et	CONHMe	Εt	Et	Εt	CONHMe
	Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
	iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
	nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
	nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
	tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
	Ph	CI	Et '	Ph	SO ₃ H	Et	Ph	Et	Н
C	H ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
C	H ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
	H ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	Cl
	H ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	Cl
С	H_2NH_2	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	Cl	Cl
	H_2NH_2	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH ₂ NH ₂	Et	Н
	H_2NH_2	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
	H_2NH_2	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
	l ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
	- CH ₂ Ph	Et	Et	CH ₂ Ph	OH	Et	CH ₂ Ph	Et	Н
	CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	Н	Н
	I ₂ CH ₂ Ph	.Ph	Ph	CH ₂ CH ₂ Ph		Ph _.	CH ₂ CH ₂ Ph	Ph	H

R ¹¹	R ¹³	· R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
H	Н	Et	Н	NO ₂	H	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	H	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Εt	Ph	Ме	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me ·	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Ме	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Εt	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Εt	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	[·] nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr \	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Εt	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	Cl	CH ₂ OMe	CI	Cl
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	CI
CH ₂ NH ₂	H.	Et	CH ₂ NH ₂	CONHMe	Et	CH_2NH_2	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
CH ₂ NHMe	Ме	Ме	CH ₂ NHMe	NO_2	Me	CH ₂ NHMe	Ме	Н
CH₂Ph	Εt	Et	CH ₂ Ph	OH	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	Н	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph	CH ₂ CH ₂ Ph	Ph	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	H	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	H	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
М́е	Н	Ph	Me	CH ₂ OH	Н	Ме	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH_2NH_2
Ме	iPr	Н	Me	ÇH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Ме	nPr	Н	Me	CH ₂ Ph	Н	Me	H	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Ме	Н	COMe
Me	tBu	Н	Ме	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	CI	Et '	Ph	SO₃H	Et	Ph	Et	H
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	H
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	H
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	Cl	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH_2NH_2	Et	Н
CH ₂ NH ₂	Η	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
CH ₂ NHMe	Me	Ме	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH₂Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	Н	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph .	CH ₂ CH ₂ Ph	Ph	H

HN-R

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO ₃ H	Н	H	Н	SO₃H
Н	Н	nBu	Н	Cl	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me ·	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et .	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Εt	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	, iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tĖu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et `	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH₂OH	CI	Ph	CH ₂ OH	ОН	Ρ'n	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH_2NH_2	Н	Et	CH_2NH_2	CONHMe	Εt	CH ₂ NH ₂	Et	Н
CH_2NH_2	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH_2NH_2	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH₂Ph	Et	Et	⊂ CH₂Ph	ОН	Εt	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph _.	CH ₂ CH ₂ Ph	Ph	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
H	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	H	Η	CI
Н	Н	tBu	H	Br	Н	Н	Н	Br
Me	.H	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Ме	CH ₂ NH ₂	Н	Ме	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Ме	Н	CH ₂ Ph
Me	nBu	Н	Ме	COMe	Н	Ме	Н	COMe
Me	tBu	Н	Me	COOH	Н	Ме	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Ęt	Εt	CONHMe
Et	Н	iPr	Εt	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph (tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO ₃ H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH₂OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	Cl
CH ₂ NH ₂	Н	Et [.]	CH ₂ NH ₂	CONHMe	Et	CH_2NH_2	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH_2NH_2	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH₂Ph	Et	Et	CH ₂ Ph	OH	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	·Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph ⁻	CH ₂ CH ₂ Ph	Ph	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	H	nPr	Н	SO₃H	H	Н	Н	SO₃H
Н	Н	_, nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Ме	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Ме	Н	CH ₂ NH ₂
Me	įPr	Н	Me	CH ₂ NHMe	Н	Ме	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Η	COOH
Et	Ph	H	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Η.	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Εt	Н
CH ₂ OH	CI	nPr√	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	Cl
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	Cl
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH_2NH_2	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
CH ₂ NHMe	Me	Ме	CH ₂ NHMe	NO_2	Me	CH ₂ NHMe	Me	Н
CH ₂ Ph	Et	Et	CH₂Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph ——	CH ₂ CH ₂ Ph	Ph	H

R11 R13 R14 R11 R13 R14 H H Et H NO2 H H H H CHO H H H NPr H SO3H H	R ¹¹ H H	R ¹³ H H	R ¹⁴
H H iPr H CHO H	H H		NO ₂
••	Н	Н	
H H nPr H SO₃H H			CHO
		Н	SO₃H
H H nBu H CI H	Н	Н	CI
H H tBu H Br H	Н	Н	Br
Me H Ph Me CH ₂ OH H	Ме	Н	CH ₂ OH
Me Et Ph Me $\mathrm{CH_2NH_2}$ H	Ме	Н	CH_2NH_2
Me iPr H Me CH ₂ NHMe H	Ме	Н	CH ₂ NHMe
Me nPr H Me CH₂Ph H	Ме	Н	CH ₂ Ph
Me nBu H Me COMe H	Ме	Н	COMe
Me tBu H Me COOH H	Me	Н	COOH
Et Ph H Et CONH ₂ H	Et	Н	CONH ₂
Et H Et Et CONHMe Et	Et	Et	CONHMe
Et H iPr Et CONHMs iPr	Et	iPr	CONHMs
iPr H nPr iPr NHMs nPr	iPr	nPr	NHMs
nPr H nBu nPr NHCOMe nBu	nPr	nBu	NHCOMe
nBu H tBu nBu $\mathrm{NO_2}$ tBu	nBu	tBu	NO_2
tBu H Ph tBu CHO Ph	tBu	Ph	Н
Ph Cl Et Ph SO ₃ H Et	Ph	Εt	Н
CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr	CH ₂ OH	nPr	Н
CH ₂ OH CI Ph CH ₂ OH OH Ph	CH ₂ OH	Ph	H
	CH ₂ OMe	CI	CI
CH ₂ OMe nPr Cl CH ₂ OMe COOH Cl	CH ₂ OMe	CI	CI
CH ₂ NH ₂ Ph Cl CH ₂ NH ₂ CONH ₂ Cl	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe Me Me CH ₂ NHMe NO ₂ Me	CH ₂ NHMe	Ме	Н
CH ₂ Ph Et Et CH ₂ Ph OH Et	CH ₂ Ph	Et	Н
CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr	CH ₂ Ph	nPr	Н
	CH ₂ CH ₂ Ph	Ph	Н

HN-R

HN-R

HN-R

		Me		
R ¹³	Х	R ¹³	X	
NO ₂	0	Me	0	
CHO	0	Et	0	
SO₃H	0	iPr	0	
CI	0	nPr	0	
Br	0	nBu	0	
CH ₂ OH	0	tBu	0	
CH ₂ NH ₂	0	Ph	0	
CH ₂ NHMe	0	CH ₂ Ph	0	
CH ₂ Ph	SO	CH ₂ CH ₂ Ph	0	
COMe	SO	Me	S	
COOH	SO	Et	S	
CONH ₂	SO	iPr	S	
CONHMe	SO	nPr	S.	
CONHMs	SO	nBu	S	
NHMs	SO	tBu	S	
NHCOMe	SO	Ph	S	
NO_2	SO2	CH ₂ Ph	S	
CHO	S	CH ₂ CH ₂ Ph	S	
SO₃H	S	Me	SO_2	
SO ₂ NHMe	SO_2	Et	SO_2	
ОН	SO	iPr	SO_2	
COMe	0	nPr	SO_2	
COOH	0	nBu	SO_2	
CONH ₂	0	tBu	SO_2	
CONHMe	0	Ph	SO_2	
CONHMs	0	CH ₂ Ph	SO_2	
.NHMs	SO_2	CH ₂ CH ₂ Ph	SO ₂	
NO_2	SO_2	Me	SO	
ОН	SO_2	Et	SO '	
COMe	SO_2	iPr	SO	
СООН	SO ₂	nPr	SO	
0				

	X	O Me	
R ¹³	Х	R ¹³	Х
NO ₂	0	Me	0
CHO	0	Et	0
SO₃H	0	iPr	0
CI	0	nPr	0
Br	0	nBu	0
CH ₂ OH	0	tBu	0
CH ₂ NH ₂	0	Ph	0
CH ₂ NHMe	0	CH₂Ph	0
CH ₂ Ph	SO	CH ₂ CH ₂ Ph	0
COMe	SO	Me	S
COOH	SO	Et	S
CONH ₂	SO	iPr	S
CONHMe	SO	nPr	S.
CONHMs	SO	nBu	S
NHMs	SO	tBu	S
NHCOMe	SO	Ph	S
NO_2	SO ₂	CH ₂ Ph	S
CHO	S	CH ₂ CH ₂ Ph	S
SO₃H	S	Me	SO_2
SO ₂ NHMe	SO_2	Et	SO_2
ОН	SO	iPr	SO_2
COMe	0	nPr	SO_2
COOH	0	nBu	SO ₂
CONH ₂	0	tBu	SO_2
CONHMe	0	Ph	SO_2
CONHMs	0	CH₂Ph	SO_2
NHMs	SO_2	CH ₂ CH ₂ Ph	SO_2
NO_2	SO_2	Me	SO
ОН	SO_2	Et	so
COMe	SO_2	iPr	SO
СООН	SO ₂	nPr	SO

		Me		
R ¹³	Х	R ¹³	Х	
NO ₂	0	Me	0	
CHO	0	Et	0	
SO₃H	0	iPr	0	
CI	0	nPr	0	
Br	0	nBu	0	
CH ₂ OH	0	tBu	0	
CH ₂ NH ₂	0	Ph	0	
CH ₂ NHMe	0	CH ₂ Ph	0	
CH ₂ Ph	SO	CH ₂ CH ₂ Ph	0	
COMe	so	Me	S	
COOH	SO	Et	S	
CONH ₂	SO	iPr	S	
CONHMe	SO	nPr	S	
CONHMs	SO	nBu	S.	
NHMs	SO	tBu	S	
NHCOMe	SO	Ph	S	
NO_2	SO_2	CH ₂ Ph	S	
CHO	S '	CH ₂ CH ₂ Ph	S	
SO ₃ H	S	Me	SO_2	
SO ₂ NHMe	SO_2	Et	SO_2	
ОН	SO	iPr	SO_2	•
COMe	0	nPr	SO_2	
COOH	0	nBú	SO_2	
CONH ₂	0	tBu	SO_2	
CONHMe	0	Ph	SO_2	
CONHMs	0	CH ₂ Ph	SO_2	
NHMs	SO_2	CH ₂ CH ₂ Ph	SO_2	
NO ₂	SO_2	Ме	SO	
ОН	SO_2	Et	SO	
COMe ·	SO_2	iPr	SO ·	
СООН	SO ₂	nPr	SO	

		Me	
R ¹³	X	R ¹³	X
NO_2	0	Me	0
CHO	0	Et	0
SO₃H	0	iPr	0
CI	0	nPr	0
Br	0	nBu	О
CH ₂ OH	0	tBu	0
CH ₂ NH ₂	0	Ph	0
CH ₂ NHMe	0	CH ₂ Ph	0
CH ₂ Ph	SO	CH ₂ CH ₂ Ph	0
COMe	SO	Me	S
COOH	SO	Et	S
CONH ₂	SO	iPr	S
CONHMe	SO	nPr	S.
CONHMs	SO	nBu	S
NHMs	SO	tBu	S
NHCOMe	SO	Ph	S
NO_2	SO ₂ (CH ₂ Ph	S
CHO	S	CH ₂ CH ₂ Ph	S
SO₃H	S	Me	SO_2
SO ₂ NHMe	SO_2	Et	SO_2
ОН	SO	iPr	SO_2
COMe	0	nPr	SO_2
COOH	0	nBu	SO_2
CONH ₂	0	tBu	SO_2
CONHMe	0	Ph	SO_2
CONHMs	0	CH ₂ Ph	SO_2
NHMs	SO_2	CH ₂ CH ₂ Ph	SO_2
NO_2	SO_2	Me	SO
OH .	SO_2	Et	SO ·
COMe	SO_2	iPr	SO
СООН	SO ₂	nPr	SO

HN-R

HN	HN OH	HN	HN
HN	HN	HN	HN N N
HN	F	HN	ő
HN	HN	HN	F HN
HN	HN	F	HN S
	HN	HN F	HN O
HN	HN	HN	HN O
HN	· · · · · · · · · · · · · · · · · · ·	ċоон -	N)
HN	HNOH	HN NH ₂	HN
HN	HN	HN	HN
HN	HN	HN Me	HN N CI
. HN	HN S	HN	HN
OH HN	HN	N	Ö
O		<u>о</u> н	

R ¹¹ HN O M	OH -Me
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\mathbf{R}^{13}	Me
R ¹¹	R ¹³
Н	Et Et
Н	iPr
Н	nPr
Н	nBu
Н	tBu
· Me ·	Ph
Me	NO ₂
Me	CHO
Me	SO ₃ H
Me	CI
Me	Br
Et	CH ₂ OH
Et	CH ₂ NH ₂
Et	CH ₂ NHMe
iPr	CH ₂ Ph
nPr	COMe
nBu	COOH '
tBu	CONH ₂
Ph	CONHMe
CH ₂ OH	CONHMs
CH ₂ OH	NHMs
CH ₂ OMe	NHCOMe
CH ₂ OMe	NO_2
CH ₂ NH ₂	CHO
CH2NH2	nPr
CH_2NH_2	CI
CH_2NH_2	F
CH ₂ NHMe	CI
CH ₂ Ph	Ęt
CH ₂ Ph	nPr
CH ₂ CH ₂ Ph	Ph

	R ¹¹ N N R ¹³	HN OH Me Me	F
_	R ¹¹	R ¹³	_
	H H	Et iPr	
	 Н	nPr	
	H	nBu	
	H	tBu	
	Me	Ph	
	Me	NO_2	
	Me	CHO	
	Me	SO₃H	
	Me	CI	
	Me	Br	
	Et	CH ₂ OH	
	Et	CH ₂ NH ₂	
	Et	CH ₂ NHMe	
	iPr	CH ₂ Ph	
	nPr	COMe	
	nBu	COOH	
	tBu	CONH ₂	
	Ph	CONHMe	
	CH ₂ OH	CONHMs	
	CH ₂ OH CH ₂ OMe	NHMs	
	CH ₂ OMe	NHCOMe NO ₂	
	CH ₂ NH ₂	CHO	
	CH ₂ NH ₂	nPr	
	CH ₂ NH ₂	Cl	
	CH ₂ NH ₂	F ·	
	CLI NILINA	01	

CH₂NHMe

CH₂Ph

CH₂Ph

CH₂CH₂Ph

CI

Et

nPr

Ph

N N	он Он
N	Me
\mathbf{R}^{13}	Me
R ¹¹	R ¹³
Н	Et
H	iPr
Н	nPr
Н	nBu
Н	tBu
Me	Ph
Ме	NO_2
Me	CHO
Me	SO₃H
Ме	CI
Ме	Br
Et	CH ₂ OH
Et	CH_2NH_2
Et	CH ₂ NHMe
iPr	CH ₂ Ph
nPr	COMe
nBu	COOH
tBu	CONH ₂
Ph	CONHMe
CH ₂ OH	CONHMs
CH ₂ OH	NHMs
CH ₂ OMe	NHCOMe
CH ₂ OMe	NO_2
CH_2NH_2	CHO
CH ₂ NH ₂	nPr
CH ₂ NH ₂	CI
CH ₂ NH ₂	F
CH ₂ NHMe	Cl
CH ₂ Ph [·]	Et
CH ₂ Ph	nPr
CH ₂ CH ₂ Ph	Ph

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	^
\mathbf{R}^{11}	HŅ ^
N-	ОН
\mathbf{N}	Me
12	O Me
R^{13}	
R ¹¹	R ¹³
Н	Et
Н	iPr
Н	nPr
Н	nBu
Н	tBu
Ме	Ph
Me	NO_2
Ме	CHO
Ме	SO₃H
Ме	CI
Me	Br
Et	CH ₂ OH
Et	CH_2NH_2
Et	CH ₂ NHMe
iPr	CH ₂ Ph
nPr	COMe
nBu	COOH '
tBu	CONH ₂
Ph	CONHMe
CH ₂ OH	CONHMs
CH ₂ OH	NHMs
CH ₂ OMe	NHCOMe
CH ₂ OMe	NO_2
CH_2NH_2	CHO
CH ₂ NH ₂	nPr
CH ₂ NH ₂	CI
CH_2NH_2	F
CH ₂ NHMe	CI
CH ₂ Ph	Et
CHDh	»D»

nPr

Ph

CH₂Ph

CH₂CH₂Ph

HN-R

HN-R

$\mathbf{o} \stackrel{\mathbf{R}^{11}}{\underset{\mathbf{R}^{12}}{\overset{\mathbf{N}}{\sim}}}$		HN OH Me Me	
	R ¹¹	R ¹²	-
	H H H	Me Et iPr	-
	H H	nPr nBu	
	Me Me	tBu Ph	
	Me Me Me	CH ₂ OH CH ₂ OMe CH ₂ NH ₂	
	Me Et	Me CH ₂ NH ₂	
	Et Et	CH ₂ NHMe CH ₂ Ph	
	iPr nPr nBu	CH ₂ Ph CH ₂ CH ₂ Ph H	
	tBu Ph	Me H	
	H ₂ OH H ₂ OH	Me Et	
Cl	H ₂ OMe H ₂ OMe	nPr Ph	
C	H ₂ NH ₂ H ₂ NH ₂ H ₂ NH ₂	H nPr Ph	
CH	H ₂ NH ₂ l ₂ NḤMe	Me Et	
C	CH ₂ Ph CH ₂ Ph ₂ CH ₂ Ph	nPr Ph CH ₂ Ph	

			F
	\mathbf{R}^{11}	$_{\rm HN}$	
	N N	↓ OH	
0=			
U	N	Me	
	R^{12}	Me	
			_
	R ¹¹	R^{12}	
	Н	Me	
	Н	Et	
	Н	iPr	
	H	nPr	
	Н	nBu	
	Me ·	tBu	
	Me	Ph	
	Ме	CH ₂ OH	
	Ме	CH ₂ OMe	
	Me	CH_2NH_2	
	Ме	Me	
•	Et	CH ₂ NH ₂	
	Et	CH ₂ NHMe	
	Et	CH ₂ Ph	
	iPr	CH ₂ Ph	
	nPr	CH ₂ CH ₂ Ph	
	nBu	H	
	tBu	Me	
	Ph	Н	
	CH ₂ OH	Me	
	CH ₂ OH	Et	
	CH ₂ OMe	nPr	•
	CH ₂ OMe	Ph	
	CH ₂ NH ₂	Н	
	CH ₂ NH ₂	nPr	
	CH ₂ NH ₂	Ph	
	· CH ₂ NH ₂	Me	
	CH ₂ NHMe	Et	
	CH ₂ Ph	nPr	
	CH ₂ Ph	Ph	
	CH ₂ CH ₂ Ph		

O=	N R ¹²	HN OH Me Me	
	R ¹¹	R ¹²	
	Н	Ме	
	Н	Et	
	Н	iPr	
	Н	nPr	
	H	nBu 🕝	
	Me ·	tBu	
	Ме	Ph	
	Me	CH ₂ OH	
	Me	CH ₂ OMe	
	Ме	CH ₂ NH ₂	
	Me	Me	
	Et	CH_2NH_2	
	Et	CH ₂ NHMe	
	Et	CH ₂ Ph	
	iPr	CH ₂ Ph	
	nPr	CH ₂ CH ₂ Ph	
	nBu	H '	
	tBu	Me	
	Ph	Н	
	CH ₂ OH	Me 	
	CH ₂ OH	Et	
	CH ₂ OMe	nPr	
	CH ₂ OMe	Ph	
	CH ₂ NH ₂	H	
	CH ₂ NH ₂	nPr	
		Ph Mo	
	CH NHM	Me ⊏₊	
	CH ₂ NHMe	Et 	
	CH ₂ Ph	nPr	
	CH ₂ Ph CH ₂ CH ₂ Ph	Ph CH ₂ Ph	
_	5/125/12/ II	<u> </u>	

		ſ	\frown
	Ľ,	HN,	~
	N	OH	
0=		Me	
	N / R ¹²	O Me	
	R ¹²		
	R ¹¹	R^{12}	
			-
	Н	Me	
	Н	Et	
	Н	iPr	
	Н	nPr	
	Н	nBu	
	Me ·	tBu	
	Me	Ph	
	Me	CH ₂ OH	
	Me	CH ₂ OMe	
	Ме	CH ₂ NH ₂	
	Me	Me	
	Et	CH ₂ NH ₂	
	Et	CH ₂ NHMe	
	Et	CH ₂ Ph	
	iPr	CH ₂ Ph	
	nPr	CH_2CH_2Ph	
	nBu	Η '	
	tBu	Me	
	Ph	Н	
	CH ₂ OH	Me	
	CH ₂ OH	Et	
	CH ₂ OMe	nPr	
	CH ₂ OMe	Ph ·	
	CH ₂ NH ₂	Н	
	CH ₂ NH ₂	nPr	
	CH ₂ NH ₂	Ph	1
	CH ₂ NH ₂	Me	
	CH ₂ NHMe	Et	
	CH ₂ Ph	nPr	
	CH ₂ Ph	Ph	
	CH ₂ CH ₂ Ph	CH ₂ Ph	_
-			-

HN-R

		Me	Me			
R ¹¹	R ¹³	R ¹¹	R ¹³			
Н	Ме	H	NO_2			
Н	Et	Н	CHO			
Н	iPr	Н	SO₃H			
Н	nPr	Н	CI			
Н	nBu	Н	Br			
Н.	tBu	Me	CH ₂ OH			
Н	Ph	Me	CH ₂ NH ₂			
Me	Me	Me	CH ₂ NHMe			
Me	Et	Me	CH ₂ Ph			
Et	iPr	Me	COMe			
Et	nPr	Me	COOH			
iPr	nBu	Et	CONH ₂			
nPr	tBu	Et	CONHMe			
nBu	Ph	Et	CONHMs			
tBu	iPr	iPr	NHMs			
Ph	nPr	nPr	NHCOMe			
CH ₂ OH	nBu 🖰	nBu	NO_2			
CH ₂ OH	tBu	tBu	CHO			
CH ₂ OMe	Ph	Ph	SO₃H			
CH ₂ OMe	Εt	CH ₂ OH	SO ₂ NHMe			
CH_2NH_2	nPr	CH ₂ OH	ОН			
CH_2NH_2	Ph	CH ₂ OMe	COMe			
CH_2NH_2	Cl	CH ₂ OMe	COOH			
CH_2NH_2	F	CH_2NH_2	CONH ₂			
CH ₂ NHMe	CI	CH ₂ NH ₂	CONHMe			
CH₂Ph	Et	CH ₂ NH ₂	CONHMs			
. CH ₂ Ph	nPr	CH_2NH_2	NHMs			
CH ₂ Ph	Ph	CH ₂ NHMe	NO_2			
CH ₂ CH ₂ Ph	Me	CH ₂ Ph	OH			
Н	CH ₂ Ph	CH ₂ Ph	COMe			
Me	CH ₂ Ph	CH ₂ CH ₂ Ph	СООН			

			<u> </u>	e
R ¹¹	R ¹³		R ¹¹	R ¹³
Н	Ме		Н	NO_2
H	Et		Н	СНО
Н	iPr		Н	SO₃H
Н	nPr		Н	CI
Н	nBu		Н	Br
H .	tBu		Me	CH ₂ OH
Н	Ph		Me	CH_2NH_2
Me	Ме		Ме	CH ₂ NHMe
Me	Et		Me	CH ₂ Ph
Et	iPr		Me	COMe
Et	nPr		Me	COOH
iPr	nBu		Et	CONH ₂
` nPr	tBu		Et	CONHMe
nBu	Ph		Εt	CONHMs
tBu	iPr		iPr	NHMs
Ph	nPr		nPr	NHCOMe
CH ₂ OH	nBu	ţ	nBu	NO ₂
CH ₂ OH	tBu		tBu	CHO
CH ₂ OMe	Ph		Ph	SO₃H
CH ₂ OMe	Et		CH ₂ OH	SO ₂ NHMe
CH_2NH_2	nPr		CH ₂ OH	ОН
CH ₂ NH ₂	Ph		CH ₂ OMe	COMe
CH ₂ NH ₂	CI		CH ₂ OMe	COOH
CH_2NH_2	F		CH ₂ NH ₂	CONH ₂
CH ₂ NHMe	CI		CH ₂ NH ₂	CONHMe
CH ₂ Ph	Et		CH ₂ NH ₂	CONHMs
. CH ₂ Ph	nPr		CH ₂ NH ₂	NHMs
CH ₂ Ph	Ph	C	CH ₂ NHMe	NO_2
CH ₂ CH ₂ Ph	Me		CH ₂ Ph	OH .
Н	CH ₂ Ph		CH ₂ Ph	COMe
Me	CH ₂ Ph	_ C	H ₂ CH ₂ Ph	СООН

R ¹¹	R ¹³		R ¹¹	R ¹³	
Н	Ме		Н	NO_2	
Н	Εt		H	CHO	
Н	iPr		Н	SO₃H	
Н	nPr		Н	CI	
Н	nBu		Н	Br	
Η .	tBu		Ме	CH ₂ OH	
Н	Ph	•	Ме	CH_2NH_2	
Me	Me		Ме	CH ₂ NHMe	
Me	Et		Ме	CH ₂ Ph	
Et	iPr		Me	COMe	
Et	nPr		Me	COOH	
iPr	nBu		Et	CONH ₂	
nPr	tBu		Et	CONHMe	
nBu	Ph		Et	CONHMs	
tBu	iPr		iPr	NHMs	
Ph	nPr		nPr	NHCOMe	
CH ₂ OH	nBu	· ·	nBu	NO_2	
CH ₂ OH	tBu		tBu	CHO	
CH ₂ OMe	Ph		Ph	SO ₃ H	
CH ₂ OMe	Et	C	CH ₂ OH	SO ₂ NHMe	
CH ₂ NH ₂	nPr	C	CH ₂ OH	ОН	
CH ₂ NH ₂	Ph	С	H ₂ OMe	COMe	
CH_2NH_2	CI	, C	H ₂ OMe	COOH	
CH ₂ NH ₂	F	C	H_2NH_2	CONH ₂	
CH ₂ NHMe	CI	С	H_2NH_2	CONHMe	
CH ₂ Ph	Et	С	H_2NH_2	CONHMs	
. CH ₂ Ph	nPr	C	H_2NH_2	NHMs	
CH ₂ Ph	Ph	CH	1 ₂ NHMe	NO_2	
CH ₂ CH ₂ Þh	Me	(CH ₂ Ph	OH	
Н	CH ₂ Ph	(CH ₂ Ph	COMe	
Ме	CH ₂ Ph	_ CH	I ₂ CH ₂ Ph	СООН	

			. IVI e	
R ¹¹	R ¹³		R ¹¹	R ¹³
Н	Me		Н	NO_2
Н	Et		Н	CHO
Н	iPr		Н	SO₃H
Н	nPr		Н	CI
Н	nBu		Н	Br
Н	tBu		Ме	CH ₂ OH
, H	Ph		Me	CH_2NH_2
Me	Ме		Ме	CH ₂ NHMe
Me	Et		Ме	CH ₂ Ph
Et	iPr		Ме	COMe
Et	nPr		Ме	COOH
iPr	nBu		Et	CONH ₂
nPr	tBu		Et	CONHMe
nBu	Ph		Et	CONHMs
tBu	iPr		iPr	NHMs
Ph	nPr		nPr	NHCOMe
CH ₂ OH	nBu	٠.	nBu	NO_2
CH ₂ OH	tBu		tBu	CHO
CH ₂ OMe	Ph		Ph	SO₃H
CH ₂ OMe	Et		CH ₂ OH	SO ₂ NHMe
CH ₂ NH ₂	nPr		CH ₂ OH	ОН
CH ₂ NH ₂	Ph	(CH ₂ OMe	COMe
CH ₂ NH ₂	CI	(CH ₂ OMe	COOH
CH ₂ NH ₂	F	(CH ₂ NH ₂	CONH ₂
CH ₂ NHMe	CI	(CH ₂ NH ₂	CONHMe
CH₂Ph	Et		CH ₂ NH ₂	CONHMs
. CH ₂ Ph	nPr	(CH ₂ NH ₂	NHMs
CH ₂ Ph	Ph		H ₂ NHMe	NO_2
CH ₂ CH ₂ Ph	Me		CH ₂ Ph	ОН
Н	CH ₂ Ph		CH ₂ Ph	COMe
Me	CH ₂ Ph	_ C	H ₂ CH ₂ Ph	СООН

HN-R

$$F_3$$
CO \xrightarrow{N} OH \xrightarrow{Me} Me

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	H	Н	CI
H	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Ме	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Ме	iPr	Н	Ме	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Ме	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
, Et	Н	Et	Et	CONHMe	Et	Εt	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu '	nBu	NO_2	tBu	nBu	tBu	NO_2H
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Εt	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	пPr	CH ₂ OH	SO ₂ NMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	OH	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	Cl	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Εt	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	'nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph	H
							•	

					•			
R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	H	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Н	Me	CH ₂ OH	Н	Ме	Н	CH ₂ OH
Me	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH_2NH_2
Me	iPr	H	Me	CH ₂ NHMe	Η	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	H	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Εt	Ph	Н	Et	CONH ₂	Н	Εt	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Εt	Et	Εt	CONHMe
Εt	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO ₂ H
tBu	Н	Ph '	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Et .	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH₂OMe	CI	CI
CH ₂ NH ₂	Ph	Cl	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et ·	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Εt	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH ₂ Ph	Εt	Et	CH ₂ Ph	OH	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH₂Ph	COMe	nPr	CH₂Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph ·	CH ₂ CH ₂ Ph	Ph	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	. R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Ме	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Ме	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH_2NH_2
Ме	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Ме	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Ме	nBu	. Н	Me	COMe	Н	Me	Н	COMe
Ме	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Εt	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	· NO ₂
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Et	Ph	Εt	H
CH ₂ OH	CI	nPr ^v	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OM		CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OM		CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	₂ Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	₂ H	Et	CH ₂ NH ₂	CONHMe	Εt	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	₂ H	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	₂ H	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHM	le Me	Me	CH ₂ NHMe	NO_2	Me	CH₂NHMe	Me	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Εt	CH ₂ Ph	Εt	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH₂Ph	nPr	Н
CH ₂ CH ₂ F	Ph Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph —	CH ₂ CH ₂ Ph	Ph	H

	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
	H	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
	Н	Н	iPr	H	CHO	Н	Н	Н	CHO
	Н	Н	nPr	H	SO₃H	Н	Н	Н	SO₃H
	Н	Н	nBu	Н	CI	Н	Н	Н	CI
	Н	Н	tBu	Н	Br	Н	Н	Н	Br
	Ме	ŀΗ	Н	Me	CH ₂ OH	Н	Ме	Н	CH ₂ OH
	Me	Et	Ph	Me	CH ₂ NH ₂	Н	Ме	Н	CH ₂ NH ₂
	Me	iPr	Н	Me	CH ₂ NHMe	Н	Ме	Н	CH ₂ NHMe
	Ме	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
	Ме	nBu	Н	Me	COMe	Н	Me	Н	COMe
	Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
	Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
	Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
	Et	Н	iPr	Et	CONHMs ·	iPr-	Et	iPr	CONHMs
	iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
	nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
	nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
	tBu	Н	Phι	tBu	CHO	Ph	tBu	Ph	Н
	Ph	CI	Et	Ph	SO₃H	Et	Ph	Et	Н
	CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
	CH ₂ OH	Cl	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
C	CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
C	CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	Cl	CH ₂ OMe	CI	CI
(CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
(CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
(CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	H
(CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	H
С	H ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Me	CH ₂ NHMe	Ме	H
-	CH ₂ Ph	Et	Et	CH₂Ph	OH	Εt	CH₂Ph	Et	Н
	CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
C	H ₂ CH ₂ Ph	·Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph	H

HN-R			·
HN /	HN OH	HN	HN
HN		HN	O N
HN	HN F		HN
HN	HN	HN	F HN N
	HN	HN	HN
HN	NH NH	HN HN	HN
HN	HN F	· F	HN O
HN	HN	HNCOOH	HN
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN	HN	HN	HN N CI
HN OH	HN S		HN
HN O	HN	N OH	

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R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO ₃ H	Н	nPr	Н	SO₃H	nPr
· H	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	Ή	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	l Ph
Et	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHN	Ле H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	Н
nBu	Н	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH ₂	
Н	Εt	Н	CONHMe	Et	H	Et	CONHM	le H
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	ls H
H	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Н	nBu	H	NHCOMe	nBu	Н	nBu	NHCOM	е н
Н	tBu	Н	NO_2	tBu	Н	tBu	NO_2	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Et	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
Cl	Ph	Н	ОН	Ph	Н	Ph	Н	COMe
Εt	Cl	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
Н	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	_. Ме	Н	NO_2	Me	Н	Ме	Н	ОН
Et	Et	Н	ОН	Εt	H	Εt	H	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	H	. Ph	H .	NO ₂

							•	
R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	H	tBu	Н	Br	tBu
Н	H	Ph	CH ₂ OH	Н	Ph	H	CH ₂ OF	ł Ph
Et	Н	. Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHN	Ле Н
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	Н
nBu	H	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	H
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH	2 H
Н	Et	Н	CONHMe	Εt	H	Et	CONHM	le H
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	ls H
H,	nPr	Н	NHMs	nPr	H	nPr	NHMs	Н
Н	nBu	H _.	NHCOMe	nBu	Н	nBu	NHCOM	le H
Н	tBu	H	NO_2	tBu	Н	tBu	NO_2	Н
H	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Εt	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO₂NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	OH	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	CI	Н	CI	Ci	COOH
nPr	CI	Н	COOH	CI	H	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Εt	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
H	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Ме	_. Me	Н	NO_2	Ме	Н	Ме	Н	ОН
Et	Et	Н	ОН	Et	H	Et	Н	COMe
nPr	nPr	Н	COMe	nPr	H	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	H 	. Ph	Н	NO ₂

R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	³ R ¹⁴	R ¹⁵
Н	. Н	Et	NO_2	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	H	SO ₃ H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	H	tBu	Н	Br	tBu
Н	·H	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	-l Ph
Et	Н	Н	CH_2NH_2	Н	Н	Н	CH ₂ NH	l ₂ H
iPr	Н	Н	CH ₂ NHMe	Н	H	Н	CH ₂ NHN	<i>I</i> le Н
nPr	H	Н	CH ₂ Ph	H	Н	Н	CH ₂ Pł	н Н
nBu	Н	H	COMe	Н	Н	Н	COMe	H
tBu	Н	Н	COOH	Н	Н	Н	COOH	I H
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH	₂ H
Н	Et	Н	CONHMe	Et ·	Н	Et	CONHM	le н
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	ls H
Н	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Η	nBu	Н	NHCOMe	nBu	Н	nBu	NHCOM	le H
Н	tBu	H,	NO_2	tBu	Н	, tBu	NO ₂ H	Н
H	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	H	SO₃H	Et	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	ОН	Ph	Н	Ph	Н	COMe
Et	CI	H	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Εt	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
H	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	Me	Н	NO_2	Ме	H	Me	Н	ОН
Et	Et	Н	ОН	Et	H	Εt	Н	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	Н	Ph	Η.	NO_2
			····					

R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	[·] H	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	Ph
Et	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHM	le H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	Н
nBu	Н	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	Н
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH ₂	Н
Н	Et	Н	CONHMe	Et	Н	Et	CONHM	е Н
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	s H
H.	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Н	nBu	H	NHCOMe	nBu	H	nBu	NHCOM	e H
Н	tBu	Η̈́	NO_2	tBu	Н	tBu	NO_2H	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Εt	Н	Εt	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	ОH	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI.	CONH ₂
Ph-	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Εt	CI	CONHMe	Εt	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
Н	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	Me	Н	NO_2	Me	Н	Mė	H	ОН
Et	Εt	Н	ОН	Et	Ĥ	Et	Н	COMe
nPr	nPr	Н	COMe	nPr	H	nPr	Н	COOH
Ph	Ph	Н	СООН	Ph	Н	Ph	H	NO ₂

HN-R HN^ HN' HN' HNÓН HN' HN. HN HN HN' HN HN F HN HN' HN' HN HN HN NH₂ ΗN HN' HN HN² HN' HNсоон HN HN HN' HN' ОΗ NH₂ HN' HN' HNHΝ̈́ Me HN' HN' HŃ. HN' HN' ÓН HN' HN' όн

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R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹	³ R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	—	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHC) iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO ₃ I	⊣ nPr
Н	Н	'nВи	CI	Н	nBu	Н	CI	nBu
H	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	H	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ C	H Ph
Εt	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ N	H_2 H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NH	lMe H
nPr	. Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ F	h H
nBu	Н	Н	COMe	Н	Н	Н	COM	е Н
tBu	Н	Н	COOH	Н	Н	Н	COO	Н Н
Ph	Н	Н	CONH ₂	Н	Н	Н	CONF	H_2 H
Н	Et	Н	CONHMe	Et	Н	Εt	CONH	Me H
Н	iPr	Н	CONHMs	iPr	H	iPi	r CONH	Ms H
Н	nPr	Н	NHMs	nPr	Н	nΡ	r NHM	s H
Н	nBu	Η,	NHCOMe	nBu	H	nΒ	u NHCO	Me H
Н	tBu	ΗÌ	NO_2	tBu	H	tΒι	ı NO ₂	Н
Н	Ph	Н	CHO	Ph	Н	Ph	ı H	SO₃H
CI	Et	Н	SO₃H	Εt	. Н	Et	H	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nΡ	r H	ОН
CI	Ph	Н	OH.	Ph	Н	Ph	ı H	COMe
Et	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Η	Et	CI	CONHMe	Et	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nΡ	r H	NHMs
H	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Ме	Ме	Н	NO_2	Ме	H _.	Me	e H	ОН
Et	Et	Н	ОН	Et	Н	Et	Н	COMe
nPr	nPr	Н	COMe	nPr	Н	nP	r H	COOH
Ph	Ph	Н	COOH	Ph	Н	·Ph	Н	NO_2

R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R, ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Ή	tBu	Br	Н	tBu	Н	Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	Ph
Εt	Н	Н	CH_2NH_2	Н	Н	Н	CH ₂ NH	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHM	le H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	Н
nBu	Н	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	Н
Ph	Н	Н	CONH ₂	Н	, H	Н	CONH ₂	Н
Н	Et	Н	CONHMe	Et	Н	Et	CONHM	е Н
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	s H
Н	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Н	nBu	Η,	NHCOMe	nBu	Н	nBu	NHCOM	е Н
Н	tBu	Н	NO_2	tBu	Н	tBu	NO_2	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Et	Н	Εt	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	OH
CI	Ph	Н	OH.	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
H	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Ме	Ме	Н	NO_2	Me	H.	Me	Н	ОН
Et	Et	Н	ОН	Et	Н	Εt	Н	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Η.	COOH
Ph	Ph	Н	COOH	Ph	Н	-Ph	Н	NO ₂

R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO ₃ H	nPr
Н	• Н	nBu	CI	H	nBu	Н	· CI	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	·H	Ph	CH ₂ OH	Н	Ph	Н	· CH ₂ OF	l Ph
Et	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHN	1e H
nPr	Н	Н	CH ₂ Ph	Н	Н	H	CH ₂ Ph	Н
nBu	Н	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	Н
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH ₂	<u>.</u> H
Н	Et	Н	CONHMe	Εt	Н	Et	CONHM	le H
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHIV	ls H
Н	nPr	Н	NHMs	nPr	Η	nPr	NHMs	Н
Н	nBu	Н	NHCOMe	nBu	Н	nBu	NHCOM	le H
Н	tBu	H'	NO_2	tBu	Н	tBu	NO ₂	Н
Н	Ph	Н	CHO	Ph	Η	Ph	Н	SO₃H
CI	Εt	Н	SO₃H	Et	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	ОН	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	CI	Н	CI	Cl	COOH
nPr	CI	H	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	Cl	CONHMe
Н	Et	CI	CONHMe	Εt	CI	Εt	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	Cl	nPr	Н	NHMs
Н	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	Me	Н	NO_2	Ме	Н	Me	Н	ОН
Et	Et	Н	ОН	Εt	Ĥ	Et	Н	COMe
nPr	nPr .	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	H	. Ph	H .	NO ₂

							*	
R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CÌ	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	H	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	Ph
Et	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH ₂	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHN	le H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	Н
nBu	Н	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	Н
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH ₂	Н
Н	Et	Н	CONHMe	Εt	H	Et	CONHM	e H
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	s H
Η.	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Н	nBu	H	NHCOMe	nBu	Н	nBu	NHCOM	е Н
Н	tBu	H [`]	NO_2	tBu	Н	tBu	NO_2	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO ₃ H
Cl	Et	Н	SO₃H	Et	Н	Εt	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	OH	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Et	Н	CONHMs
H	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
H	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	_. Ме	Н	NO_2	Me	H	Ме	Н	ОН
Et	Et	Н	ОН	Et	H	Et	H	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	H .	COOH
Ph	Ph	H	СООН	Ph	Н	. Ph	Н	NO ₂

LINID			
HN-R			
HN	HN OH	HN	HN
HN		HN	O
HN	HN		HN N
HN	HN	HN	F HN N
	HN	HN	HN N
HN	NH	HN HN	HN S
HN	HN	· Ė	HN
HN	HN	HN COOH	HN
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN	HN	HN	HN N CI
HN OH	HN		HN
HN O	HN	N OH	

Me Et Ph Me CH_2NH_2 H Me H CH_2NH_3 H Me H CH_2NH_3 H Me H CH_3NH_3 H Me H CH_3NH_3 H Me H CH_3NH_3 H Me H Me CH_4NH_3 H Me H Me CH_4NH_3 H Me H Me $COMe$ H Me H Me $COMe$ H Me H Me $COOH$ H Me H Et $COOH$ H Et H Et $COOH$ Et $COOH$ H IPR OF OOH IPR OT OOH IPR OF OOH IPR OF OOH IPR OT OOH	R ¹⁴ NO ₂ CHO
H H iPr H CHO H H H H H nPr H SO ₃ H H H H H H nBu H Cl H Me H Ph Me CH ₂ OH H Me H Me iPr H Me CH ₂ NHMe H Me H Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et CO Et H iPr Et CONHMs iPr Et iPr O nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	_
H H NPr H SO ₃ H H H H H H NBu H CI H H H H H H H H H H H H H H H H H H H	CHO
H H nBu H Cl H H H H H tBu H Br H H H Me H Ph Me CH ₂ OH H Me H Me Et Ph Me CH ₂ NH ₂ H Me H C Me iPr H Me CH ₂ NHMe H Me H Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et C iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	
H H tBu H Br H H H Me H Ph Me CH ₂ OH H Me H Me Et Ph Me CH ₂ NH ₂ H Me H C Me iPr H Me CH ₂ NHMe H Me H C Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et C Et H iPr Et CONHMs iPr Et iPr C iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	SO₃H
Me H Ph Me CH ₂ OH H Me H Me Et Ph Me CH ₂ NH ₂ H Me H Me iPr H Me CH ₂ NHMe H Me H C Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et C Et H iPr Et CONHMs iPr Et iPr C iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	CI
Me Et Ph Me CH ₂ NH ₂ H Me H C Me iPr H Me CH ₂ NHMe H Me H C Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHME Et Et Et C Et H iPr Et CONHMS iPr Et iPr C iPr H nPr iPr NHMS nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	Br
Me iPr H Me CH ₂ NHMe H Me H C Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et C Et H iPr Et CONHMs iPr Et iPr C iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	
Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHME Et Et Et C Et H iPr Et CONHMS iPr Et iPr C iPr H nPr iPr NHMS nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	CH ₂ NH ₂
Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHME Et Et Et C Et H iPr Et CONHMS iPr Et iPr C iPr H nPr iPr NHMS nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	H₂NHMe
Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHME Et Et Et C Et H iPr Et CONHMS iPr Et iPr C iPr H nPr iPr NHMS nPr iPr nPr nPr H nBu nPr NHCOME nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	CH ₂ Ph
Et Ph H Et CONH ₂ H Et H Et Et CONHMe Et Et Et CONHMe Et Et Et CONHMe Et Et Et CONHMS iPr Et iPr CONHMS iPr Et iPr CONHMS iPr H nPr iPr NHMS nPr iPr nPr nPr nPr nPr nPr nPr nPr nPr nPr n	COMe
Et H Et Et CONHMe Et Et C Et H iPr Et CONHMs iPr Et iPr C iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	COOH
Et H iPr Et CONHMs iPr Et iPr C iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	CONH ₂
iPr H nPr iPr NHMs nPr iPr nPr nPr nPr n Pr n Pr n Pr n Pr n Bu n Pr n Bu n Pr n Bu n	ONHMe
nPr H nBu nPr NHCOMe nBu nPr nBu N nBu H tBu nBu NO ₂ tBu nBu tBu	ONHMs
nBu H tBu nBu NO ₂ tBu nBu tBu	NHMs
1.24	HCOMe
tBu H Ph tBu CHO Ph tBu Ph	NO_2
tou one in the	H
Ph Cl Et Ph SO ₃ H Et Ph Et	Н
CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	Н
CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph	Н
CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI	CI
CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI	CI
CH ₂ NH ₂ Ph Cl CH ₂ NH ₂ CONH ₂ Cl CH ₂ NH ₂ Cl	CI
CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et CH ₂ NH ₂ Et	H
CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr CH ₂ NH ₂ nPr	Н
CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph CH ₂ NH ₂ Ph	Н
CH ₂ NHMe Me Me CH ₂ NHMe NO ₂ Me CH ₂ NHMe Me	Н
CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph Et	Н
CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr	Н
CH ₂ CH ₂ Ph Ph Ph CH ₂ CH ₂ Ph COOH Ph CH ₂ CH ₂ Ph Ph	Η

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	•	R ¹¹	R ¹³	R ¹⁴
H	H	Et	Н	NO ₂	Н		Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н		Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н		Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н		Н	Н	CI
Н	Н	tBu	Н	Br	Н		Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н		Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н		Ме	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н		Ме	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н		Me	H	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н		Me	H	COMe
Me	tĖu	Н	Me	COOH	Н		Me	H	COOH
Et	Ph	Н	Εt	CONH ₂	Н		Et	Н	CONH ₂
Εt	Н	Et	Et	CONHMe	Et		Et	Εt	CONHMe
Εt	Н	iPr	Et	CONHMs	iPr		Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr		iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu		nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu		nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph		tBu	Ph	Н
Ph	CI	Et '	Ph	SO ₃ H	Et		Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr		CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	(CH ₂ OH	Ph	Н
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	Cl	С	H ₂ OMe	CI	Cl
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	Cl	С	H ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	C	H ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	C	H ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	C	H ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	C	H ₂ NH ₂	Ph	, Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO ₂	Me	CH	H ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	(CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr		CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph 	CH —	I ₂ CH ₂ Ph	Ph	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Ęt	Н	NO ₂	Н		Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CĬ	Н	Н	Н	CĪ
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	H	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	H	CONH ₂
Et	Н	Εt	Et	CONHMe	Et	Et	Εt	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Η	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Η	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	CI	Et	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	Cl	nPr ,	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	H
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	Cl
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Εt	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH_2NH_2	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Ме	CH ₂ NHMe	NO ₂	Me	CH ₂ NHMe	Ме	Н
CH₂Ph	Εt	Εt	CH ₂ Ph	OH	Et	CH ₂ Ph	Et	Н
CH₂Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph	Н
								

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	H	Cl
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	. Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBù	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
₽h	CI	Et '	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	Cľ	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	Cl	CH ₂ NH ₂	CONH ₂	Cl	CH_2NH_2	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH_2NH_2	Et	H
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Мe	Н
CH₂Ph	Et	Et	CH₂Ph	OH	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	.Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph	H

HN-R

					 _	
R ¹³	R ¹⁴		R ¹³	R ¹⁴	 R ¹³	R ¹⁴
Н	Me		NO ₂	Н	 OMe	Н
Н	Et		CHO	Н	OEt	Н
Н	iPr		SO₃H	Н	OiPr	Н
Н	nPr		CI	Н	OnPr	Н
Н	nBu		Br	Н	OBn	Н
Н	tBu		CH ₂ OH	Н	OPh	Н
H	Ph		CH_2NH_2	Н	SMe	Н
Me	Н		CH ₂ NHMe	Н	SEt	H
Εt	H H		CH ₂ Ph	Н	SiPr	Н
iPr	Н		COMe	Н	SnPr	Н
nPr	Н		COOH	Н	OCH ₂ CH ₂ P	h H
nBu	Н		CONH ₂	H	SCH ₂ CH ₂ P	h H
tBu	Н		CONHMe	Et	H	OMe
Ph	NO_2		CONHMs	iPr	Н	OEt
Н	CHO		NHMs	nPr	CI	OiPr
Н	SO₃H ,		NHCOMe	nBu	Me	OnPr
Н	Cl		NO ₂	tBu	Et	OBn
Н	Br		CHO	Ph	nPr	OPh
Н	CH ₂ OH		SO₃H	Et	Ph	SMe
Н	CH ₂ NH ₂		SO ₂ NHMe	nPr	Me	SEt
CI	CH ₂ NHMe		OH	Ph	Et	SiPr
CI	CH ₂ Ph		COMe	CI	nPr	SnPr
CI	COMe		COOH	Cl	Ph	OCH ₂ CH ₂ Ph
Et	COOH		CONH ₂	CI	NO_2	SCOMe
nPr	CONH ₂		CONHMe	Εt	CHO	OMe
Ph	CONHMe		CONHMs	nPr	SO₃H	OEt
. Н	CONHMs		NHMs	Ph	CI	OnPr
Н	. NHMs		NO_2	Me	Br	SMe
Н	NHCOMe		ОН	Et	CH ₂ OH	SEt
Me	CO ₂ H		COMe	nPr	CH_2NH_2	SiPr
Et	Н	_	СООН	Ph	 . F	SPh
-						

R ¹³	R ¹⁴	R ¹³	R ¹⁴	R ¹³	R ¹⁴
Н	Me	NO ₂	Н	OMe	Н
Н	Et	CHO	Н	OEt	Н
Н	· iPr	SO₃H	Н	OiPr	Н
. Н	nPr	CI	Н	OnPr	Н
Н	nBu	Br	Н	OBn	Н
Н	[†] tBu	CH ₂ OH	Н	OPh	Н
Н	Ph	CH ₂ NH ₂	Н	SMe	Н
Ме	Н	CH ₂ NHMe	Н	SEt	Н
Et	Н	CH ₂ Ph	Н	SiPr	Н
iPr	Н	COMe	Н	SnPr	Н
nPr	Н	COOH	Н	OCH ₂ CH ₂ Ph	Н
nBu	» H	CONH ₂	Н	SCH ₂ CH ₂ Ph	H
tBu	Н	CONHMe	Ėt	H C	Ме
Ph	NO_2	CONHMs	iPr	Η (DEt
H	CHO	NHMs	nPr	CI C)iPr
Н	SO₃H	NHCOMe	nBu	Me O	nPr
Н	CĬ	NO_2	tBu	Et C)Bn
Н	Br	CHO	Ph	nPr C	Ph
Н	CH ₂ OH	SO₃H	Εt	Ph S	Ме
Н	CH ₂ NH ₂	SO ₂ NHMe	nPr	Me S	SEt
.CI	CH ₂ NHMe	OH	Ph	Et S	SiPr
CI	CH ₂ Ph	COMe	CI	nPr S	nPr
CI	COMe	COOH	CI	Ph OCH ₂	₂ CH ₂ Ph
Et	COOH	CONH ₂	Cl	NO ₂ SC	ОМе
nPr	CONH ₂	CONHMe	Et		Ме
Ph	CONHMe	CONHMs	nPr	SO ₃ H C	DEt
· H	CONHMs	NHMs	Ph	CI O	nPr
Н	, NHMs	NO_2	Ме		Ме
Н	NHCOMe	ОН	Εt	-	SEt
Ме	CO ₂ H	COMe	nPr		iPr
Et	Н	СООН	Ph	. F S	Ph

R ¹³	R ¹⁴	R	¹³ R	14	R ¹³	R ¹⁴
Н	Me	NO	D_2 I	1	OMe	Н
Н	Et	CH	10 I	1	OEt	Н
Н	iPr	SO	₃ H I	1	OiPr	Н
Н	nPr	C	i I	1	OnPr	Н
Н	nBu	В	r l	1	OBn	Н
Н	tBu	CH ₂	OH H	ł	OPh	Н
Н	Ph	CH ₂	NH ₂ I	1	SMe ·	Н
Ме	Н	CH ₂ N	HMe H	1	SEt	Н
Et	Н	CH ₂	Ph ł	1	SiPr	Н
iPr	Н	CO	Me H	1	SnPr	Н
nPr	Н	CO	HC HC	1	OCH ₂ CH ₂ P	h H
nBu	Н	COI	NH ₂ F	1	SCH ₂ CH ₂ P	h H
tBu	Н	CON	HMe E	it .	Н	OMe
Ph	NO_2	CON	HMs iF	Pr -	Н	OEt
Н	CHO	NH	Ms nl	^o r	CI	OiPr
Н	SO₃H	NHC	OMe nE	Bu	Me	OnPr
Н	Cl	NO	O_2 tE	u	Et	OBn
Н	Br	CH	IO P	h	nPr	OPh
Н	CH ₂ OH	so	₃ H E	t	Ph.	SMe
Н	CH ₂ NH ₂	SO ₂ N	HMe n	Pr -	Ме	SEt
CI	CH ₂ NHMe	Ol	H P	h	Et	SiPr
CI	CH ₂ Ph	CO	Vie C	1	nPr	SnPr
CI	COMe	CO	OH C	1	Ph	OCH ₂ CH ₂ Ph
Et	COOH	CON	NH ₂ C	I	NO_2	SCOMe
nPr	CONH ₂	CON	-lMe E	t	CHO	OMe
Ph	CONHMe	CON	HMs nl	Pr	SO₃H	OEt
. H	CONHMs	NHI	Ms P	h	CI	OnPr
Н	NHMs	NC	O_2 M	е	Br	SMe
Н	NHCOMe	OI	-l E	t ·	CH ₂ OH	SEt
Me	CO ₂ H	CO	Vie nf	^o r	CH ₂ NH ₂	SiPr
Et	Н	CO	OH P	h	F	SPh

	R ¹³	R ¹⁴		R ¹³	R ¹⁴		R ¹³	R ¹⁴
	Н	Me		NO ₂	Н		ОМе	Н
	Н	Et		CHO	Н		OEt	Н
	Н	iPr		SO₃H	Н		OiPr	Н
	Н	nPr		CI	Н		OnPr	Н
	Н	nBu		Br	Н		OBn	Н
	Н	tBu		CH ₂ OH	Н		OPh	Н
	Н	Ph		CH_2NH_2	H		SMe	Н
	Me	Н		CH ₂ NHMe	Н		SEt	Н
	Et	, H		CH ₂ Ph	H	2)	SiPr	Н
	iPr	Н		COMe	Н		SnPr	H
	nPr	Н		COOH	Н		OCH ₂ CH ₂ F	Ph H
	nBu	Н		CONH ₂	Н		SCH ₂ CH ₂ P	h H
	tBu	Н		CONHMe	Ét		H	OMe
	Ph	NO_2		CONHMs	ŀiPr		Н	OEt
	Н	CHO		NHMs	nPr		CI	OiPr
	Η	SO₃H (NHCOMe	nBu		Me	OnPr
	Н	CI		NO_2	tBu		Et	OBn
•	Н	Br		CHO	Ph		nPr	OPh
	Н	CH ₂ OH		SO₃H	Et		Ph	SMe
	Н	CH ₂ NH ₂		SO ₂ NHMe	nPr		Ме	SEt
	CI	CH ₂ NHMe		OH	Ph		Εt	SiPr
	CI	CH ₂ Ph		COMe	CI		nPr	SnPr
	CI	COMe		COOH	CI		Ph	OCH ₂ CH ₂ Ph
	Et	COOH		CONH ₂	CI		NO_2	SCOMe
	nPr	CONH ₂		CONHMe	Et		CHO	OMe
	Ph	CONHMe		CONHMs	nPr		SO₃H	OEt
	· H	CONHMs		NHMs	Ph		CI	OnPr
	Н	. NHMs		NO_2	Ме		Br	SMe
	Н	NHCOMe		ОН	Et		CH ₂ OH	SEt
	Ме	CO ₂ H		COMe	nPr		CH ₂ NH ₂	SiPr
	Et	Н		COOH	Ph		. F	SPh
	•		_		~~~~			

HN-R

			^
	$ \mathbf{R}^{11} $	HŅ	<u>`</u>
o _{\infty}	✓N ✓	ОН	
י ז		Me	
R^{12}	'\	O Me	
	Ö		
	R ¹¹	R ¹²	
	Н	Me	
	Н	Et	
	Н	iPr	
	Н	nPr	
	Н	nBu	
	Me	tBu	
	Me	Ph	
	Ме	CH ₂ OH	
	Me	CH ₂ OMe	
	Ме	CH ₂ NH ₂	
	Me	Me	
	Et	CH ₂ NH ₂	
	Et -	CH ₂ NHMe	
	Et	CH ₂ Ph	
	iPr	CH ₂ Ph	
	nPr	CH ₂ C _H ₂ Ph	
	nBu	H	
	tBu	Me	
	Ph	H	
	CH₂OH CH₂OH	Me Et	
	CH ₂ OMe	nPr	•
	CH ₂ OMe	Ph	
	CH ₂ NH ₂	H	
	CH ₂ NH ₂	nPr	
	CH ₂ NH ₂	Ph	
	CH ₂ NH ₂	Me	
	CH ₂ NHMe	Et	
	CH ₂ Ph	nPr	
	CH ₂ Ph	Ph	
	CH ₂ CH ₂ Ph		

		F	F
	\mathbf{R}^{11}	HN \	
0	N	OH	
o		OH	
12 / N		Me	
R^{12}	0	Me	
			_
	R ¹¹	R ¹²	
			
	Н	Me	
	Н	Et	
	Н	iPr	
	Н	nPr	
	Н	nBu	
	Me	tBu	
	Me	Ph	
	Me	CH ₂ OH	
	Me	CH ₂ OMe	
	Me	CH ₂ NH ₂	
	Me	Me	
	Et	CH ₂ NH ₂	
	Et	CH ₂ NHMe	
	Et	CH ₂ Ph	
	iPr -	CH ₂ Ph	
	nPr	CH ₂ CH ₂ Ph	
	nBu	H	
	tBu	Me 	
	Ph	H	
	CH ₂ OH	Me	
	CH ₂ OH	Et	•
	CH ₂ OMe	nPr	
	CH ₂ OMe	Ph	
	CH ₂ NH ₂	Н	
	CH ₂ NH ₂	nPr	
		Ph Mo	
	CH ₂ NH ₂	Me ⊏+	
	CH Ph	Et nPr	
	CH ₂ Ph CH ₂ Ph	Ph	
	CH ₂ CH ₂ Ph	CH ₂ Ph	

R ¹¹	R ¹²
Н	Me
Н	Et
Н	iPr
Н	nPr
H	nBu
Me	tBu
Me	Ph
Me	CH ₂ OH
Me	CH ₂ OMe
Me	CH ₂ NH ₂
Me	Me
Et	CH ₂ NH ₂
Et	CH ₂ NHMe
Et	CH ₂ Ph
iPr	CH ₂ Ph
nPr	CH ₂ CH ₂ Ph
nBu	Н
tBu	Me
Ph	Н
CH ₂ OH	Me
CH ₂ OH	Et
CH ₂ OMe	nPr
CH ₂ OMe	Ph
CH_2NH_2	Н
CH_2NH_2	nPr
CH_2NH_2	Ph
CH_2NH_2	Me
CH ₂ NHMe	Et
CH ₂ Ph	nPr
CH ₂ Ph	Ph
CH ₂ CH ₂ Ph	CH ₂ Ph

			^
		[/ \
$ \mathbf{R}^{1} $	1	HŅ ^	<u>\</u>
$0 \searrow N$	<u> </u>	ОН	
N.		Me	
R^{12}	/ //	O Me	
_ <u>ö</u>		1710	
	R ¹¹	R ¹²	
	Н	Me	
	Н	Et	
	Н	iPr	
	Н	nPr	
	Н	nBu	
	Me	tBu	
	Me	Ph	
	Ме	CH ₂ OH	
	Ме	CH ₂ OMe	
	Ме	CH ₂ NH ₂	
	Ме	Me	
	Et	CH ₂ NH ₂	
	Et	CH ₂ NHMe	
	Et	CH ₂ Ph	
	iPr	CH ₂ Ph	
	nPr	CH ₂ CH ₂ Ph	
	nBu	H	
	tBu .	Me	
0	Ph	H	
	H ₂ OH	Me	
	H ₂ OH	Et "D"	
	l ₂ OMe	nPr Ph	
	l ₂ OMe l ₂ NH ₂	Ph H	
	121 V 112 12NH2	nPr	
	121 VI 12 12NH ₂	Ph	
	121VI 12 12NH ₂	Me	
	NHMe	Et	
-	H ₂ Ph	nPr	
	H ₂ Ph	Ph	
	_	CH₂Ph	

HN-R

R ¹¹ O. N.	HN
	OH
o N	Me Me
\mathbf{R}^{12}	Me
R ¹¹	R ¹²
Н	Me
Н	Et
. Н	iPr
Н	nPr
Н	nBu
Me ·	tBu
Me	Ph
Me	CH ₂ OH
Me	CH ₂ OMe
Me	CH ₂ NH ₂
Ме	Me
Et	CH ₂ NH ₂
Et	CH ₂ NHMe
Et	CH ₂ Ph
iPr	CH ₂ Ph
nPr	CH ₂ CH ₂ Ph
nBu	H '
tBu	Me
Ph	Н
CH ₂ OH	Me
CH ₂ OH	Et
CH ₂ OMe	nPr
CH ₂ OMe	Ph
CH_2NH_2	Н
CH ₂ NH ₂	nPr
CH ₂ NH ₂	Ph
CH ₂ NH ₂	Ме
CH ₂ NHMe	Et
CH ₂ Ph	nPr
CH ₂ Ph	Ph
CH ₂ CH ₂ Ph	CH ₂ Ph

			F
	\mathbf{R}^{11}	HŅ ^	
0,	N N	↓ OH	
7		/ _M .	
0	Ň	Me Me	
	\mathbf{R}^{12}	Me	
•		10	_
	R ¹¹	R ¹²	-
			<u> </u>
	H 	Me	
	H	Et	
	H	iPr	
	H	nPr	
	H	nBu	
	Me	tBu	
	Me	Ph	
	Me	CH ₂ OH	
	Ме	CH ₂ OMe	
	Ме	CH ₂ NH ₂	
	Me	Me	
	Et	CH ₂ NH ₂	
	Et	CH ₂ NHMe	
	Et :D::	CH ₂ Ph	
	iPr	CH ₂ Ph	
	nPr	CH ₂ CH ₂ Ph	
	nBu	H	
	tBu	Me	
	Ph	H	
	CH ₂ OH	Me	
	CH ₂ OH	EtD.	•
	CH ₂ OMe	nPr	
	CH ₂ OMe	Ph H	
	CH ₂ NH ₂	nPr Ph	
	CH ₂ NH ₂ CH ₂ NH ₂	Me	
	CH ₂ NHMe	Et	
		⊑ι nPr	
	CH ₂ Ph	Ph	
	CH ₂ CH ₂ Ph		

	W
R ¹¹	R ¹²
Н	Ме
Н	Et
Н	iPr
Н	nPr `
Н	nBu
Me	tBu
Me	Ph
Me	CH ₂ OH
Ме	CH ₂ OMe
Me	CH ₂ NH ₂
Me	Me
Et	CH ₂ NH ₂
Et	CH ₂ NHMe
Et	CH ₂ Ph
iPr	CH ₂ Ph
· nPr	CH ₂ CH ₂ Ph
nBu	Ηι
tBu	Me
Ph	Н
CH ₂ OH	Ме
CH ₂ OH	Et
CH ₂ OMe	nPr
CH ₂ OMe	Ph
CH ₂ NH ₂	H
CH ₂ NH ₂	nPr
CH ₂ NH ₂	Ph
CH ₂ NH ₂	Me
CH ₂ NHMe	Et
CH ₂ Ph	nPr
CH ₂ Ph	Ph
CH ₂ CH ₂ Ph	CH ₂ Ph

o/	R ¹¹ N N R ¹²	HN OH Me Me	
	R ¹¹	R ¹²	
	Н	Ме	
	Н	Et	
	Н	iPr	
	Н	nPr	
	H	nBu	
	Me ·	tBu	
	Me	Ph	
	Me	CH ₂ OH	
	Me	CH ₂ OMe	
	Me	CH_2NH_2	
	Me	Me	
	Et	CH ₂ NH ₂	
	Et	CH ₂ NHMe	
	Et 	CH ₂ Ph	
	iPr	CH ₂ Ph	
	nPr	CH ₂ CH ₂ Ph	
	nBu	H	
	tBu	Me 	
	Ph	H	
	CH ₂ OH	Me	
	CH ₂ OH CH ₂ OMe	Et ~D~	
	CH ₂ OMe	nPr Ph	
	CH ₂ NH ₂	H	
	CH ₂ NH ₂	nPr	
	CH ₂ NH ₂	Ph	
	CH ₂ NH ₂	Me	
	CH ₂ NHMe	Et	
	CH ₂ Ph	nPr	
	CH ₂ Ph	Ph	
	CH ₂ CH ₂ Ph	CH ₂ Ph	

HN-R

			<u>. </u>
HN	HN	HN	HN
HN	ÓН	HN	Ö
HN	HN F		HN N
HN .	HN	HN	F HN N
	HN	HN	HN
HN	NH	HN HN	HN S
HN	HN F	F	HN
HN	HN	HNCOOH	HN
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN .	HN	HN	HN N CI
HN OH	HN		HN
HN O	HN	N OH	

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	H	—	NO ₂
Н	H	iPr	Н	CHO	H	Н	Н	CHO
Н	H	nPr	Н	SO₃H	Н	Н	Н	SO ₃ H
Н	Н	nBu	Н	CI	Η .	Н	H	Cl
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	H	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Ме	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	H	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu '	nBu	NO ₂	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Ме	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH ₂ Ph	Et	Et	CH ₂ Ph ·	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	'nРr	nPr	CH ₂ Ph	COMe	nPr'	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph	CH ₂ CH ₂ Ph	Ph	Н

	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	•	R ¹¹	R ¹³	R ¹⁴
	Н	Н	Et	Н	NO ₂	Н	•	H	Н	NO ₂
	Н	Н	iPr	Н	CHO	Н	,	Н	Н	CHO
	Н	Η	nPr	Н	SO₃H	Н		H	Н	SO₃H
	Н	Η	nBu	Н	CI	Н		H	Н	CI
	Н	Н	tBu	Н	Br	Н		Н	Н	Br
	Me	ŀΗ	Н	Me	CH ₂ OH	Н		Me	Н	CH ₂ OH
	Me	Et	Ph	Me	CH ₂ NH ₂	H		Me	Н	CH ₂ NH ₂
	Me	iPr	Н	Me	CH ₂ NHMe	Н		Me	Н	CH ₂ NHMe
	Me	nPr	Н	Me	CH ₂ Ph	Н		Me	Н	CH ₂ Ph
	Me	nBu	Н	Me	COMe	Н		Me	Η	COMe
	Me	tBu	Н	Me	COOH	Н		Ме	Н	COOH
	Et	Ph	Н	Et	CONH ₂	Н		Et	Н	CONH ₂
	Et	Н	Et	Et	CONHMe	Et		Et	Et	CONHMe
	Et	Н	iPr	Et	CONHMs	iPr		Et	iPr	CONHMs
	iPr	H	nPr	iPr	NHMs	nPr		iPr	nPr	NHMs
	nPr	Η	nBu	nPr	NHCOMe	nBu		nPr	nBu	NHCOMe
	nBu	Н	tBu	nBu	NO_2	tBu		nBu	tBu	NO_2
	tBu	Η	Ph '	tBu	CHO	Ph		tBu	Ph	Н
	Ph	CI	Et	Ph	SO₃H	Εt		Ph	Et	Н
	CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	C	CH ₂ OH	nPr	Н
	CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	C	CH ₂ OH	Ph	Н
(CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	C	H ₂ OMe	CI	CI
(CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	C	H ₂ OMe	CI	CI
(CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	С	H_2NH_2	CI	CI
(CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	С	H ₂ NH ₂	Εt	Н
(CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	С	H_2NH_2	nPr	Н
(CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	С	H_2NH_2	Ph	Н
С	H ₂ NHMe	Me	Ме	CH ₂ NHMe	NO_2	Ме	CH	l₂NHMe	Me	H
	CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	C	CH ₂ Ph	Et	Н
	CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	C	CH ₂ Ph	nPr	Н
C -	H ₂ CH ₂ Ph	`Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph [·]	CH —	₂ CH ₂ Ph	Ph	H

$$\begin{array}{c|c} R^{11} & HN \\ \hline S & N & OH \\ \hline R_{13} & O & Me \\ \hline R_{14} & O & Me \\ \end{array}$$

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	· NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO ₃ H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	Cl	Н	Н	H	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	H	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Ме	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Εt	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Εt	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Εt	Ph	SO₃H	Εt	Ph	Et	Н
CH ₂ OH	CI	nPr '	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ρ'n	CH ₂ OH	Ph	Н
CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Εt	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph	CH ₂ CH ₂ Ph	Ph	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	H	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	H	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	CI
H	Н	tBu	H	Br	H	H	Н	Br
Me	H	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH_2NH_2
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Εt	Н	iPr	Εt	CONHMs	i Pr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO ₂	tBu	nBu	tBu	NO_2
tBu	Н	Ph 🔻	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Εt	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	H
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	Cl
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	Cl	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et ·	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	H
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Ме	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Et	CH₂Ph	OH	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ρh	Ph	CH ₂ CH ₂ Ph	COOH	Ph·	CH ₂ CH ₂ Ph	Ph	Н

HN-R

HN	HNOH	HN	HN
HN	HN F	HN	HN O
HN	HN	HN	F HN N
HN	HN	HN	HN
HN	HN	2 HN F	HN S
HN	HN	ни соон	HN O
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN	HN	HN	HN N CI
HNOH	HN		HN
HN O	HN	HNOH	

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	———	Н	H	NO ₂
Н	Н	iPr	Н	CHŌ	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	· H	CI
Н	Н	tBu	H	Br	Н	Н	Н	Br
Ме	ŀΗ	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Ме	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Ме	nPr	Н	Ме	CH ₂ Ph	H	Me	Н	CH ₂ Ph
Ме	nBu	Н	Me	COMe	Н	Me	Н	COMe
Ме	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Εt	Et	Εt	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph √	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Et	Н
CH ₂ OH		nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH		Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
		CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
		CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂		CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	-	Εt	CH ₂ NH ₂	CONHMe	Εt	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	₂ H	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	₂ H	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	H
CH ₂ NHM		Me	CH ₂ NHMe	NO_2	Ме	CH₂NHMe	Me	Н
CH ₂ Ph	Et	Et	CH₂Ph	ОН	Εt	CH ₂ Ph	Et	H
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ P	h 'Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph [.]	CH ₂ CH ₂ Ph	Ph	Н

							•	
R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	H	Н	Н	Br
Me	ŀΗ	Н	Me	CH ₂ OH	Н	Ме	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Ме	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Ме	Н	CH ₂ NHMe
Me	nPr	Н	Ме	CH ₂ Ph	Н	Ме	Н	CH ₂ Ph
Me	nBu	Н	Ме	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Εt	Ph	Н	Et	CONH ₂	Н	Et	Η	CONH ₂
Εt	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Εt	Н	iPr	Et	CONHMs	i Pr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph 🤇	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	H
CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	Cl	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH_2NH_2	Εt	H
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH_2NH_2	nPr	H
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	H
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
ĊH₂Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	H
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	·Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph·	CH ₂ CH ₂ Ph	Ph	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	H	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	H	Н	Br
Me	H	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Мe	Et	Ph	Me	CH ₂ NH ₂	H	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Ме	CH ₂ NHMe	Н	Me	H	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Ме	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Ме	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Εt	H	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	H
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Et	Н
CH ₂ OH	CI	nPr⊸	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Εt	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph.	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
H ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Et	CH₂Ph	OH	Et	CH ₂ Ph	Et	, H
CH ₂ Ph	nPr	nPr	CH₂Ph	COMe	nPr	CH ₂ Ph	nPr	Н
H ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph	CH ₂ CH ₂ Ph	Ph	Н

Me nPr H Me CH_2Ph H Me H CH_2Ph Me nBu H Me $COMe$ H Me H $COMe$ Me tBu H Me $COOH$ H Me $COOH$ Et $COOH$ H Et $COOH_2$ H Et $COOH_2$									
H H H IPF H CHO H H H CHO H H H NPF H SO₃H H H H SO₃H H H H NBU H CI H H H H CI H H H BU H BF H H H BF Me H CH₂OH H Me H CH₂OH Me Et H M Me CH₂NH₂ H Me H CH₂NH₂ Me iPF H Me CH₂NHØ H Me H CH₂NH₂ Me nPF H Me CH₂Ph H Me H CH₂NH₂ Me nBU H Me COMe H Me H CH₂Ph Me nBU H Me COMH H Me H COMH Me tBU H ME COMH H ME H COMH Et Ph H Et CONH₂ H Et H CONH₂ Et H ET CONHMS iPF Et iPF CONHMS iPF H NPF iPF NHMS nPF iPF nPF NHMS iPF H NPF iPF NHCOMH NBU NPF NHMS iPF H NBU NPF NHCOMH NBU NPF NHMS nPF H NBU NPF NHCOMH NBU NPF NHMS nBU H tBU NBU NO₂ tBU NBU tBU NO₂ tBU H DP TBU CH₂OH OP H TH Ph CI Et Ph SO₃H Et Ph Et H CH₂OH CI NPF CH₂OH OP H TH CH₂OH CI NPF CH₂OH OP H TH CH₂OH CI NPF CH₂OH OP H TH CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OMH ET CH₂OH OP H TH CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OMH NPF CH₂OH OP H TH CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OMH TP CH₂OH OP TH CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OMH TP CH₂OH OP TH CH₂OH CI CH₂OMH COMH TP CH₂OMH CI CI CH₂OMH NPF CH₂OH OP TH CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OMH PP CH₂OH OP TH CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OMH TP CH₂OH OP TH CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OH CI CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OH CI CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OH CI CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OH CI CI CI CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OH CI CI CI CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OH CI CI CI CH₂OH CI CH₂OMH COMH CI CH₂OMH CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OMH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OMH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OMH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OMH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CI CH₂OMH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OMH CI CH₂OH CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OMH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CI CH₂O	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ^{1,4}	R ¹¹	R ¹³	R ¹⁴
H H H nBu H Cl H H H Cl H H H Br H H H Cl H H H H Br H H H Cl H H H H Br H H H H Br Me H H H Me CH₂OH H Me H CH₂OH Me Et Ph Me CH₂NH₂ H Me H CH₂NH₂ Me iPr H Me CH₂NHMe H Me H CH₂NHMe Me nPr H Me CH₂NHMe H Me H CH₂NHMe Me nBu H Me COMe H Me H CH₂Ph Me tBu H Me COMH H Me H COOH Et Ph H Et CONH₂ H Et H CONH₂ Et H Et Et CONHMB Et Et Et Et CONHMB iPr H nPr iPr NHMS nPr iPr nPr NHMS iPr H nBu nPr NHCOMe nBu nPr nBu NHCOME nBu H tBu nBu NO₂ tBu nBu tBu NO₂ tBu H Ph tBu CHO Ph tBu Ph H CH₂OH Cl Et Ph SO₃H Et Ph Et H CH₂OH Cl CH₂OH SO₂NHME nPr CH₂OH nPr H CH₂OH Cl CH₂OH COOH Cl CH₂OH Cl Cl CH₂OME Et Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂OME TT Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂OME TT Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂OME COOH Cl CH₂OME Cl Cl CH₂NH₂ Ph Cl CH₂NH₂ CONHME Et CH₂NH₂ Et H CH₂NH₂ H nPr CH₂NH₂ NHMS Ph CH₂NH₂ Ph H CH₂NHWE ME ME CH₂NHME NO₂ ME CH₂NHME ME H CH₂Ph Et Et CH₂Ph OH Et CH₂Ph nPr H	Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
H H H BBU H CI H H H BF Me H H H Me CH₂OH H Me H CH₂OH Me Et Ph Me CH₂NHMe H Me H CH₂NHMe Me nPr H Me CH₂NHMe H Me H CH₂NHMe Me nPr H Me CH₂Ph H Me H CH₂Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COOH Et Ph H Et CONHME Et Et Et CONHME Et H iPr Et CONHME iPr Et iPr CONHMS iPr H nPr iPr NHMS nPr iPr nPr NHMS nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu NO₂ tBu nBu tBu NO₂ tBu H Ph tBu CHO Ph tBu Ph H CH₂OH CI Et Ph SO₃H Et Ph Et H CH₂OH CI nPr CH₂OH SO₂NHMe nPr CH₂OH nPr H CH₂OH CI CH₂OH COOH CI CH₂OH CI CI CH₂OME Et CH₂OH COOH CI CH₂OH CI CI CH₂OME TE CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CI CH₂OH CI CI CH₂OH COOH CI CH₂OH CI CI CH₂OH CI CI CI CH₂OH CI CI CI CH₂OH COOH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CI CH₂OH CI CI CI C	Н	Н	iPr	Н	CHO	Н	Н	H	CHO
H H H H H H H Br H H H Br H H CH20H H Me H CH20H H Me H CH20H H Me H CH2NH2 H Me H CH2NH3 Me H CH2NH3 H Me H CH2NH3 H Me H CH2NH3 H Me H CH2Ph H Me H CH2Ph H Me H CH2Ph H Me H CH2Ph CH2Ph Me H CH2Ph CONH Bu H CONH Bu DE T CONH Bu	Н	Н	nPr	H	SO₃H	Н	Н	Н	SO₃H
Me H H Me CH2OH H Me H CH2OH Me iPr H Me CH2NH2 H Me H CH2NH2 Me iPr H Me CH2NHMe H Me H CH2NHMe Me nPr H Me CH2Ph H Me H CH2Ph Me nBu H Me COMe H Me H CH2Ph Me nBu H Me COMe H Me H CH2Ph Me nBu H Me COMe H Me H CH2Ph Me nBu H Me COMe H Me H CH2Ph COMe H CM2Ph CM2Ph H COMH COMH H COMH H COMH COMH Et Et Et CONHMB IP IP NHMS IP <t< td=""><td>Н</td><td>Η</td><td>nBu</td><td>Н</td><td>CI</td><td>Н</td><td>Н</td><td>Н</td><td></td></t<>	Н	Η	nBu	Н	CI	Н	Н	Н	
Me Et Ph Me CH ₂ NH ₂ H Me H CH ₂ NH ₂ Me iPr H Me CH ₂ NHMe H Me H CH ₂ NHMe Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H CM ₂ Ph Me nBu H Me COMe H Me H CM ₂ Ph Me nBu H Me COMe H Me H CM ₂ Ph Me nBu H Me COMe H Me H COMe COMe H COMe H COMe H COMe COMe H COMe H COMe COMe H COMe COMe COMe DR T T T NHCOMe NHCOME NHCOME NHCOME NHCOME NHCOME NHCOME <	Н	Н	tBu	Н	Br	Н	Н	H	Br
Me iPr H Me CH2NHMe H Me H CH2NHMe Me nPr H Me CH2Ph H Me H CH2Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COMe Me tBu H Me COOH H Me H COMe Me tBu H Me COOH H Me H COOH Et Ph H Et COOH H Me H COOH Et Ph H Et COOH H Et Et COOH Me NO	Me	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COMe Me tBu H Me COOH H Me H COOH Me tBu H Me COOH H Me H COOH Et Ph H Et COOH H Me H COOH Et Ph H Et COOH H Et Et COOH COOH Me Me NPr COOH COOH Me NPr	Me	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	H	CH ₂ NH ₂
Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COOH Et Ph H Et CONH2 H Et H COOH Et Ph H Et CONHMB Et Et H CONHMB Et H iPr Et CONHMB iPr Et CONHMB iPr NHMS nPr nPr NHMS nNPr NHMS nNPr NHMS NNPr NHMS NNPr NPR NHMS NNPr NPR NPR NPR NPR NPR <td>Me</td> <td>iPr</td> <td>Н</td> <td>Me</td> <td>CH₂NHMe</td> <td>Н</td> <td>Me</td> <td>Н</td> <td>CH₂NHMe</td>	Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me tBu H Me COOH H Me H COOH Et Ph H Et CONH ₂ H Et H CONH ₂ Et H Et Et CONHMe Et Et H CONHMe Et H H Et Et CONHMe Et Et CONHMe Et H H IPr Et CONHMe IPr NHMs NHCOME INDR NHCOME INDR NHCOME INDR NHCOME INDR NHCOME INDR IPr CONHMs IPr IPr NHMS NHCOME INDR INDR NHCOME INDR INDR <td>Me</td> <td>nPr</td> <td>Н</td> <td>Me</td> <td>CH₂Ph</td> <td>Н</td> <td>Me</td> <td>Н</td> <td>CH₂Ph</td>	Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Et Ph H Et CONH ₂ H Et H CONH ₂ Et H Et Et CONHMe Et Et Et CONHMe Et H IPr Et CONHMe IPr Et IPr CONHMe IPr H IPr Et CONHMe IPr Et IPr CONHMe IPr H IPr Et CONHMe IPr Et IPr CONHMe IPr H nPr IPr NHCOMe IPr IPr NHMs NPr IPr NHMs NPr NHMs NHCOME IPr	Me	nBu	Н	Me	COMe	H	Me	Н	COMe
Et H Et Et CONHMe Et Et Et CONHMe Et H ET CONHME ET H IP' CONHMS IP' ET IP' CONHMS IP' ET IP' CONHMS IP' ET IP' CONHMS IP' ET IP' CONHMS IP' NHMS IP' IP' NHMS IP' NH	Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et H iPr Et CONHMS iPr Et iPr CONHMS iPr H nPr iPr NHMS nPr iPr nPr NHMS nPr iPr nPr NHMS nPr iPr nPr NHMS nPr H nBu nPr NHCOMe nBu nPr nBu NHCOME nBu H tBu nBu NO2 tBu nBu tBu NO2 tBu nBu tBu NO2 tBu nBu tBu NO4 tBu Ph H Ph CI Et Ph SO3H Et Ph Et H CH2OH CI nPr CH2OH SO2NHME nPr CH2OH nPr H CH2OH CI CH2OME COME CI CH2OME CI CI CH2OME Et CI CH2OME COME CI CH2OME CI CI CH2OME nPr CI CH2OH CI CH2OME COME CI CH2OME CI CI CH2NH2 Ph CI CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H Et CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H nPr CH2NH2 CONHMS nPr CH2NH2 nPr H CH2NH2 H nPr CH2NH2 NHMS Ph CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NHME ME CH2NHME ME CH2PH OH Et CH2PH NPr H CH2PH NPr CH2PH OH Et CH2PH NPr H CH2PH NPr H CH2PH NPr H CH2PH NPr H CH2PH NPr C	Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
iPr H nPr iPr NHMs nPr iPr nPr NHMs nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu NO2 tBu nBu tBu NHCOMe nBu H tBu nBu NO2 tBu nBu tBu NHCOMe tBu H Ph tBu CHO Ph tBu nBu tBu NHCOMe tBu H Ph tBu NHO2 tBu nBu tBu NHCOMe tBu H Ph tBu CHO Ph tBu NHO2 tBu NHCOME NHCOME <td>Et</td> <td>Н</td> <td>Et</td> <td>Et</td> <td>CONHMe</td> <td>Et</td> <td>Et</td> <td>Εt</td> <td>CONHMe</td>	Et	Н	Et	Et	CONHMe	Et	Et	Εt	CONHMe
nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu nBu NO2 tBu nBu tBu NO4 tBu Ph H Ph CI Et Ph SO3H Et Ph Et H CH2OH CI nPr CH2OH SO2NHME nPr CH2OH nPr H CH2OH CI CH2OME CI CI CH2NH2 Ph CI CH2NH2 CONHME Et CH2NH2 CI CI CH2NH2 H Et CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H nPr CH2NH2 CONHMS nPr CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NHME ME CH2NHME NO2 ME CH2NHME ME H CH2PH Et CH2PH OH Et CH2PH Et H CH2PH NPr CH2PH OH Et CH2PH Et H CH2PH NPr CH2PH OH Et CH2PH NPr H CH2PH NPr CH2PH NPr CH2PH NPr CH2PH NPr H CH2PH NPr CH2PH NPr H CH2PH NPr CH2PH NPr CH2PH NPr H CH2PH NPr CH2PH NPr CH2PH NPr H CH2PH NPr CH2PH NPr CH2PH NPr H CH2PH NPr CH	Et	Н	iPr	Et	CONHMs	· iPr	Et	iPr	CONHMs
nBu H tBu nBu NO2 tBu nBu tBu NO2 tBu nBu tBu NO2 tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO3H Et Ph Et H CH2OH CI nPr CH2OH SO2NHMe nPr CH2OH nPr H CH2OH CI Ph CH2OH OH Ph CH2OH Ph H CH2OH CI CI CH2OME COME CI CH2OME CI CI CH2OME CI CI CH2OME CI CI CH2OME CI CI CH2NH2 Ph CI CH2NH2 CONH2 CI CH2NH2 CI CI CH2NH2 TH Et CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H Ph CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H Ph CH2NH2 CONHMS nPr CH2NH2 NPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NH2 NHMS Ph CH2NH2 Ph H CH2NHME ME CH2NHME ME CH2PH Pr CH2PH CH2PH NPr CH2PH CH2PH NPr CH2PH COME NPr CH2PH NPr H CH2PH NPr CH2PH COME NPr CH2PH NPr H CH2PH NPr CH2PH COME NPr CH2PH NPr H	iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
tBu H Ph tBu CHO Ph tBu Ph H Ph Ph CH2NH2 Ph Et H CH2NH2 H Ph CH2Ph Ph CH2Ph Ph CH2Ph Ph Et H CH2Ph Ph CH2Ph Ph CH2Ph Ph H CH2Ph Ph H Et CH2Ph Ph CH2Ph Ph H CH2PH Ph CH2PH Ph H CH2PH Ph H CH2PH Ph CH2PH Ph H CH2PH Ph H CH2PH Ph CH2PH Ph CH2PH Ph Ph Ph CH2PH Ph Ph Ph Ph CH2PH Ph	nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
Ph CI Et Ph SO $_3$ H Et Ph Et H CH $_2$ OH OH Ph CH $_2$ OH Ph H CH $_2$ OH OH Ph CH $_2$ OH Ph H CH $_2$ OH Ph CH $_2$ OH Ph H CH $_2$ OM CI CI CI CH $_2$ OMe COMe CI CH $_2$ OMe CI	nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	tBu	Н	Ph 、	tBu	CHO	Ph		Ph	H
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Ph	CI	Et	Ph	SO₃H	Et	Ph	Εt	H
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	·CI		CI	CI
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CH ₂ NH ₂	H	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NHMe Me Me CH ₂ NHMe NO ₂ Me CH ₂ NHMe Me H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph Et H CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr H	CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
$\mathrm{CH_2Ph}$ Et Et $\mathrm{CH_2Ph}$ OH Et $\mathrm{CH_2Ph}$ Et H $\mathrm{CH_2Ph}$ nPr nPr $\mathrm{CH_2Ph}$ nPr H	CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	H
CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr H	CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Me	CH ₂ NHMe	Me	Н
_	CH₂Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Εt	H
CH ₂ CH ₂ Ph Ph Ph CH ₂ CH ₂ Ph COOH Ph CH ₂ CH ₂ Ph Ph H	CH₂Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
	CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph .	CH ₂ CH ₂ Ph	Ph	H

HN-R

HN-R

ш	NI.	p

HN-Me	HN	HN HN
HNEt	HN	HN OH HN
HN		
HN	HN	HN
HN .	HN	HN HN F
HN	HN	HN. HN F
HN	HN	Me N
HN		HN HN
HN	· HN	HN HN
HN	HN	HN
HN	HN	HN HN
HN	HN	$HN \longrightarrow N \longrightarrow HN \longrightarrow S \longrightarrow M$
HNOH	HN	$HN \longrightarrow 0$ $HN \longrightarrow 0$
HN	THY	

HN-R

HN-R

HN SO₃H	OMe	Me HN Me
H ₂ NO ₂ S	MeOCO	OMe
CH ₂ OH	NHCOOEt	HNOMe
HN	HN	OMe
COCH ₃	HN	ÓMe
CI	OCOCH ₃	HN NO ₂
HN	Me	OMe
HN	HN OH	HN COMe
HN	HN	HN Br
HN	OH Br	HN

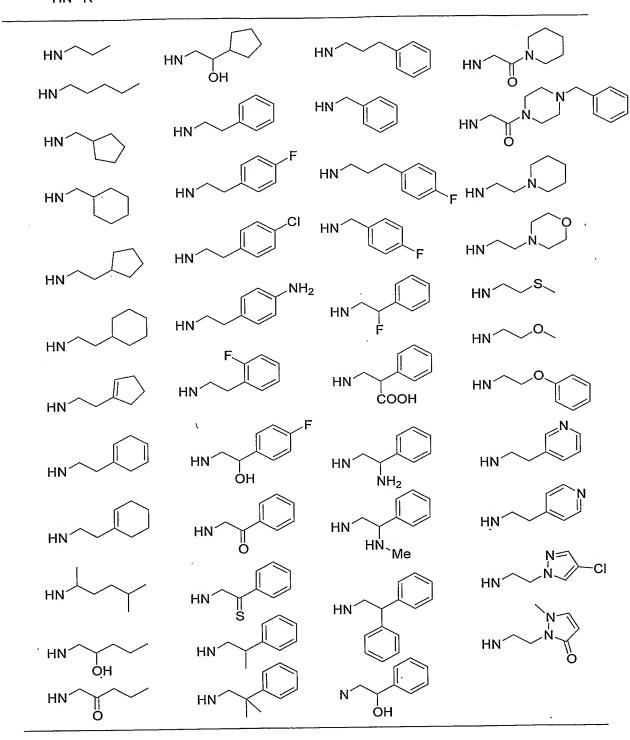
HN-R

-	IN	 R
_	IIN	 г

HN-R			
HN	HN	HN	HN N
HN N-N	HN	HN	HN N
HN N	HN	HN	HN N
HN N	HN N	HN	HŅ
HN N CI	HN CI	HN	HN
N N		o O	HN
HN	HN N	ΓŃ	HN
HN	HN	HN N-S	
HN	HN N H	HN	HN N N
HN	HN	- HN S	HN N

HN-R

HN-R



HN-R

HN ·	HNOH	HN	HN
HN	HN	HN	HN
HN	HN	HN	F HN
	HN	HN	HN
HN	HN	HN F	HN O
HN	HN	HN COOH	HN
HN	HN	HN HN	HN
HN	ÓH HN	NH ₂	HN
HN	ö	HN Me	HN N CI
· HN	HN	HN	HN
HN → ÓH	HN	N OH	·

HN-R

HN-R

HN	HN OH	HN	HN
HN	HN	HN	HN O N
HN	HN	HN	F HN N
	HN	HN	HN
HN	HN	HN	HN S
HN	HN F	F HN	HN
HN		соон	N
HN	HNOH	HN NH ₂	HN N
HN	HN	HN HN Me	HN N CI
HN	HN	HN	HN
HNOH	HN		HN O .
HN	HN	N OH	

HN	HN OH	HN	$HN \longrightarrow N$
HN	S.		O
HN	HN F	HN	HN N
HN	HN	HN	F HN ^ ^
	HN	HN	HN
HN	NH	2	HN
HN	HN E.	HN F	HN
HN	HN	HN COOH	HN
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN	HN	HN	HN N CI
. HN OH	HN		HN
HN O	HN	N OH	•

HN-R

ŀ	HN /	HNOH	HN	$HN \longrightarrow N$
Н	N		HN	HN N N
i	HN \	HN F	HN	Ö
I	HN N	HN	HN	F HN O
. 1	HN \	HN	F	HN S
	HN	HN	HN F	HN O
	HN	HN	HNCOOH	HN
		HN	F	HN
	HN	ОН	HN NH ₂	N
	HN	HN	HN HN Me	HN N CI
1	HN	HN	HN	HN N
٠	HNOH	HN		ни
S-1-7	HN	HN HN	NOH	

				
R ¹³	R ¹⁴	R ¹³	R ¹⁴	R ¹³ R ¹⁴
Me	·Et	Н	ОН	H CH₂OH
Me	iPr	Н	OMe	H CH ₂ NH2
Me	nPr	Me	OEt	H CH ₂ NHMe
Me	nBu	Et	OCF ₃	H CH₂Ph
Ме	tBu	iPr	OnPr	Me CH ₂ CH ₂ Ph
Et ·	Me	Ph	OiPr	Me COMe
iPr	Et	Н	Ph	Me COOH
nPr	´ iPr	Me	SEt	Me CONH ₂
nBu	nPr	Et	SiPr	Me CONHMe
tBu	nBu	iPr	NH_2	Et CONHMs
OMe.	Н	Н	NHMe	Et NHMs
OEt	Me	Н	NHEt	Et NHCOMe
OiPr	Et	Н	NHPh	Et NO ₂
OPh	iPr	CH ₂ OH	Me	iPr CHO
SEt	Н	CH ₂ NH2	Et	iPr SO₃H
SiPr	Me	CH ₂ NHMe	iPr	iPr SO ₂ NHMe
NH_2	Н	CH ₂ Ph	Н	· iPr OH
NHMe	Me	CH ₂ CH ₂ Ph	Н	NHMs CI
NHEt	Ph	COMe	Н	NHCOMe CI
NHPh	Н	COOH	H	NO ₂ CI
CI	Me	CONH ₂	Н	CHO Br
CI	Et	CONHMe	Н	SO₃H Br
Cl	Ph ·	CONHMs	Ме	SO ₂ NHMe Br
Me	CI	NHMs	Me	OH Br
Et	CI	NHCOMe	Me	CI NHMs
Ph	CI	NO_2	Me	CI NHCOMe
· Br	Ме	CHO	Et	CI NO ₂
Br ຸ	CI	SO₃H	Et	Br CHO
Me	Br	SO ₂ NHMe	Et	Br SO₃H
CI	Br	ОН	Et	Br SO ₂ NHMe

R ¹³	R ¹⁴		R ¹³	R ¹⁴	R ¹³	R ¹⁴	
Me	Et		Н	ОН	 Н	CH ₂ OH	
Me	iPr		H	OMe	Н	CH ₂ NH2	
Me	nPr		Me	OEt	Н	CH ₂ NHMe	
Me	nBu		Et	OCF ₃	Н	CH ₂ Ph	
Me	tBu		iPr	OnPr	Ме	CH ₂ CH ₂ Ph	
Et	Me		Ph	OiPr	Me	COMe	
iPr	Εt		Н	Ph	Ме	COOH	
nPr	iPr		Me	SEt	Ме	CONH ₂	
nBu	nPr		€t	SiPr	Ме	CONHMe	
tBu	nBu		iPr	NH_2	Et	CONHMs	
OMe	Н		Н	NHMe	Et	NHMs	
OEt	Ме		Н	NHEt	Et	NHCOMe	
OiPr	Et		Н	NHPh	Et	NO ₂	
OPh	iPr		CH ₂ OH	Me	iPr	CHO	
SEt	Н		CH ₂ NH2	Et	iPr	SO₃H	
SiPr	Ме	ξ	CH ₂ NHMe	iPr	iPr	SO ₂ NHMe	
NH_2	Н		CH ₂ Ph	Н	iPr	ОН	
NHMe	Ме		CH ₂ CH ₂ Ph	Н	NHMs	s CI	
NHEt	Ph		COMe	Н	NHCON	/le Cl	
NHPh	Н		COOH	Н	NO_2	CI	
CI	Мe		CONH ₂	Н	CHO	Br	
CI	Et		CONHMe	Н	SO₃H	Br	
CI	Ph		CONHMs	Me	SO ₂ NHI	Me Br	
Me	CI		NHMs	Me	ОН	Br	
Et	CI		NHCOMe	Me	CI	NHMs	
. Ph	CI		NO_2 .	Me	CI	NHCOMe	
Br	Ме		CHO	Et	CI	NO_2	
Br ·	Cl		SO₃H	Et	Br	CHO	
Ме	Br		SO ₂ NHMe	Et	Br	SO₃H	
CI	Br		ОН	Et	 Br	SO ₂ NHMe	

R ¹³	R ¹⁴	R ¹³	R ¹⁴	R ¹³ R ¹⁴
Me	Et	Н	ОН	H CH ₂ OH
Me	iPr	Н	OMe	H CH ₂ NH2
Me	nPr	Me	OEt	H CH ₂ NHMe
Me	nBu	Et	OCF ₃	H CH ₂ Ph
Me	tBu	iPr	OnPr	Me CH ₂ CH ₂ Ph
Et	Ме	Ph	OiPr	Me COMe
iPr	Et	Н	Ph	Me COOH
nPr	iPr	Me	SEt	Me CONH ₂
nBu	nPr	Et	SiPr	Me CONHMe
tBu	nBu	iPr	NH_2	Et CONHMs
OMe	Н	Н	NHMe	Et NHMs
OEt	Ме	Н	NHEt	Et NHCOMe
OiPr	Et	Н	NHPh	Et NO ₂
OPh	iPr	CH ₂ OH	Ме	iPr CHO
SEt	Н	CH ₂ NH2	Et	iPr SO₃H
SiPr	Ме	CH ₂ NHMe	iPr	iPr SO ₂ NHMe
$^{\circ}NH_{2}$	Н	CH ₂ Ph	Н	iPr OH
NHMe	Me	CH ₂ CH ₂ Ph	Н	NHMs CI
NHEt	Ph	COMe	Н	NHCOMe CI
NHPh	Н	COOH	Н	NO ₂ CI
CI	Me	CONH ₂	Н	CHO Br
CI	Et	CONHMe	Н	SO₃H Br
CI	Ph	CONHMs	Me	SO ₂ NHMe Br
Ме	CI .	NHMs	Ме	OH Br
Et	Cl	NHCOMe	Me	CI NHMs
Ph	CI	NO_2	Me	CI NHCOMe
Br	Me	CHO	Et	CI NO ₂
. Br	CI	SO ₃ H	Et	Br CHO
Me	Br	SO ₂ NHMe	Et	Br SO₃H
CI	Br -	ОН	Et ·	Br SO ₂ NHMe

R ¹³	R ¹⁴	R ¹³	R ¹⁴	R ¹³ R ¹⁴
Me	Et	Н	ОН	H CH ₂ OH
Me	iPr	Н	OMe	H CH ₂ NH2
Me	nPr	Me	OEt	H CH ₂ NHMe
Me	nBu	Et	OCF ₃	H CH₂Ph
Ме	tBu	iPr	OnPr	Me CH ₂ CH ₂ Ph
Et	· Me	Ph	OiPr	Me COMe
iPr	Et	Н	Ph	Me COOH
nPr	iPr	Me	SEt	Me CONH ₂
nBu	nPr	Et	SiPr	Me CONHMe
tBu	nBu	iPr	NH_2	Et CONHMs
OMe	Н	Н	NHMe	Et NHMs
OEt	Me	Н	NHEt	Et NHCOMe
OiPr	Et	Н	NHPh	Et NO ₂
OPh	iPr	CH ₂ OH	Me	iPr CHO
SEt	Н	CH ₂ NH2	Et	iPr SO ₃ H
SiPr	Me	CH ₂ NHMe	iPr	iPr SO ₂ NHMe
NH_2	H	CH ₂ Ph	Н	iPr OH
NHMe	Me	CH ₂ CH ₂ Ph	H	NHMs Cl
NHEt	Ph	COMe	Н	NHCOMe CI
NHPh	Η .	COOH	Н	NO ₂ CI
CI	Me	CONH ₂	Н	CHO Br
CI	Et	CONHMe	Н	SO₃H Br
CI	Ph	CONHMs	Me	SO ₂ NHMe Br
Me	CI	NHMs	Me	OH Br
Et	CI	NHCOMe	Me	CI NHMs
Ph	CI	NO_2	Me	CI NHCOMe
· Br	Ме	CHO	Et	CI NO ₂
Br .	CI	SO₃H	Et .	Br CHO
Me	Br	SO ₂ NHMe	Et	Br SO₃H
CI	Br	ОН	Et	Br SO ₂ NHMe

	_		_			
R ¹³	R ¹⁴		R ¹³	R ¹⁴		R ¹³ R ¹⁴
Me	Et		Н	ОН		H CH ₂ OH
Me	iPr		Н	OMe		H CH ₂ NH2
Me	nPr	•	Me	OEt		H CH ₂ NHMe
Me	nBu		Et .	OCF ₃		H CH ₂ Ph
Me	tBu		iPr	OnPr		Me CH ₂ CH ₂ Ph
Et	Ме		Ph	OiPr		Me COMe
iPr	Et		Н	Ph		Me COOH
nPr	iPr		Me	SEt		Me CONH ₂
nBu	nPr		Et	SiPr		Me CONHMe
tBu	nBu		iPr	NH_2		Et CONHMs
OMe	Н		Н	NHMe		Et NHMs
OEt	Ме		Н	NHEt		Et NHCOMe
OiPr	Et		Н	NHPh		Et NO ₂
OPh	iPr		CH ₂ OH	Me		iPr CHO
SEt	Н		CH ₂ NH2	Et		iPr SO ₃ H
SiPr	Me		CH ₂ NHMe	iPr		iPr SO ₂ NHMe
NH_2	Н	ţ	CH ₂ Ph	Н		iPr OH
NHMe	Ме		CH ₂ CH ₂ Ph	Н		NHMs Cl
NHEt	Ph		COMe	Н		NHCOMe CI
NHPh	Н		COOH	Н		NO ₂ CI
CI	Ме		CONH ₂	Н		CHO Br
CI	Et		CONHMe	Н		SO₃H Br
CI	Ph		CONHMs	Me		SO ₂ NHMe Br
Me	CI		NHMs	Me		OH Br
Et	Cl		NHCOMe	Me		CI NHMs
Ph	Cl		NO_2	Me		CI NHCOMe
· Br	Me		CHO	Et		NO_2
Br .	CI		SO₃H	Et		Br CHO
Me	Br		SO ₂ NHMe	Et	•	Br SO₃H
CI	Br		ОН	Et		Br SO ₂ NHMe

R¹³ R¹³ R¹³ R¹³ R¹³ R¹³ Me Et H OH H CH₂OH Me iPr H OMe H CH₂OH Me iPr H OMe H CH₂OH Me iPr Me OEt H CH₂OH Me iPr Me OEt H CH₂OH Me iBu iPr OnPr Me COMe iPr Et Me Ph OiPr Me COMe iPr Et H Ph Me COMe COMe iPr Et H Ph Me COMe COMe IPr Me COMe IPr IPr Me COMe IPr IPr Me COMe IPr IPr Me COMe IPr IPr </th <th></th> <th></th> <th></th> <th></th> <th></th>					
Me iPr H OMe H CH₂NH2 Me nPr Me OEt H CH₂NHMe Me nBu Et OCF₃ H CH₂NHMe Me nBu iPr OnPr Me CH₂CH₂Ph Me tBu iPr OnPr Me COMe iPr Et Me Ph OiPr Me COMe nBu nPr Et SiPr Me CONH₂ CONH₂ nBu nPr Et SiPr Me CONHMe CONH₄ tBu nBu iPr NH₂ Et CONHMe Et CONHMe Et CONHMe H NHMs NHMs OOH H NHCOME H NHCOME H NHCOME De NHCOME NHMs NO₂ NHMMs NHM NHMs NHMs NHMs NHMs NHMs NHMS NHMS NH NHMS NH NHMS	R ¹³	R ¹⁴	R ¹³	R ¹⁴	R ¹³ R ¹⁴
Me nPr Me OEt H CH₂NHMe Me nBu Et OCF₃ H CH₂Ph Me tBu iPr OnPr Me CH₂CH₂Ph Et Me Ph OiPr Me COMe iPr Et Me Ph Me COMe iPr Et H Ph Me COOH nPr iPr Me SEt Me CONH₂ nBu nPr Et SiPr Me CONHMe CONHMe tBu nBu iPr NH₂ Et CONHMs CONHMs Et NHCOME CONHMs Et NHCOME CONHMs Et NHCOME CHOOH NHCOME	Me	Et	Н	ОН	H CH ₂ OH
Me nBu Et OCF3 H CH2Ph Me tBu iPr OnPr Me CH2CH2Ph Et Me Ph OiPr Me COMe iPr Et Me Ph Me COMe iPr Et H Ph Me COMe nPr iPr Me SEt Me CONH2 nBu nPr Be SiPr Me CONHMe CONHMe nBu nPr Et SiPr Me CONHMs CONHMs Me CONHMs OND2 DONHMs DOND2 DOND3	Me	iPr	Н	OMe	H CH ₂ NH2
Me tBu iPr OnPr Me CH ₂ CH ₂ Ph Et Me Ph OiPr Me COMe iPr Et H Ph Me COOH nPr iPr Me SEt Me CONH ₂ nBu nPr Et SiPr Me CONHMe tBu inBu iPr NH ₂ Et CONHMS OMe H H NHME Et NHMS OEt Me H NHEt Et NHCOME OiPr Et H NHPh Et NO ₂ OPh iPr CH ₂ OH Me iPr CHO SEt H CH ₂ NH2 Et iPr SO ₃ H SiPr Me CH ₂ NHMe iPr iPr SO ₂ NHMe NH ₂ H CH ₂ Ph H iPr OH NHME ME CH ₂ CH ₂ Ph H NHMS CI NHET Ph COME H NHCOME CI NHPh H COOH H NO ₂ CI CI Me CONH ₂ H CHO Br CI Et CONHMS Me SO ₂ NHME Br Me CI NHMS Me OH Br Et CI NHMS Me OH Br Et CI NHCOME OH OPP ET CHO ON OPP ON OPP ON ON OPP ON OPP ON ON OPP ON ON OPP ON ON OPP ON ON ON OPP ON ON ON OPP ON ON ON ON OPP ON OPP ON O	Me	nPr	Me	OEt	
Et Me Ph OiPr Me COMe iPr Et H Ph Me COOH nPr iPr Et H Ph Me SEt Me CONH2 nBu nPr Et SiPr Me CONHME tBu nBu iPr NH2 Et CONHMS OME H NHET ET NHCOME OiPr Et H NHPh Et NHCOME OiPr Et H NHPh Et NHCOME OiPr Et H NHPh Et NO2 OPh iPr CH2OH Me iPr CHO SET H CH2NHME iPr IPr SO3H SIPr Me CH2NHME iPr IPr SO2NHME NH2 H CH2Ph H IPr OH NHMS CI NHET Ph COME H NHCOME CI NHPh H COOH H NHCOME CI NHPh H COOH H NHCOME CI NHPH H COOH H NO2 CI CI ET CONHME H SO3H Br CI NHMS ME CI NHMS Ph CI NHCOME ME CI NHCOME BR ME CHO ET CI NO2 ME CI NHCOME BR ME CHO ET CI NO2 ME CI NHCOME BR ME CHO ET CI NO2	Me	nBu	Et	OCF ₃	Ĥ CH₂Ph
iPr Et H Ph Me COOH nPr iPr Me SEt Me CONH ₂ nBu nPr Et SiPr Me CONHMe tBu nBu iPr NH ₂ Et CONHMs OMe H H H NHMe Et NHMS OEt Me H NHEt Et NHCOME OiPr Et H NHPh Et NO ₂ OPh iPr CH ₂ OH Me iPr CHO SEt H CH ₂ NH2 Et iPr SO ₃ H SiPr Me CH ₂ NHMe iPr iPr SO ₂ NHMe NH ₂ H CH ₂ Ph H iPr OH NHME Me CH ₂ CH ₂ Ph H NHCOME CI NHET Ph COME H NHCOME CI NHPh H COOH H SO ₃ H Br CI Et CONHME H SO ₃ H Br CI Ph CONHMS ME SO ₂ NHME Br ME CI NHMS ME CI NHMS ME CI NHCOME ME CI NHMS Ph CI NO ₂ ME CI NHCOME Br Me CHO Et CI NHCOME Br Me CHO Et CI NHCOME Br Me CHO Et CI NHCOME Br CI SO ₃ H Et Br CHO ME Br CI SO ₃ H Et Br CHO	Me	tBu	iPr	OnPr	Me CH ₂ CH ₂ Ph
nPr iPr iPr Me SEt Me CONH ₂ nBu nPr Et SiPr Me CONHMe tBu nBu iPr NH ₂ Et CONHMs OMe H H NHME Et NHMS OEt Me H NHEt Et NHCOME OiPr Et H NHPh Et NO ₂ OPh iPr CH ₂ OH Me iPr CHO SEt H CH ₂ NH iPr SO ₃ H SiPr Me CH ₂ NHMe iPr iPr SO ₂ NHMe NH ₂ H CH ₂ Ph H iPr OH NHME ME CH ₂ CH ₂ Ph H NHMS CI NHET Ph COME H NHCOME CI NHPh H COOH H NO ₂ CI CI Me CONH ₂ H CHO Br CI Et CONHME H SO ₃ H Br CI Ph CONHMS ME SO ₂ NHME Br Me CI NHMS ME OH Br Me CI NHMS ME OH Br Me CI NHMS ME OH Br Me CI NHCOME ME CI NHCOME Br Me CHO Et CI NHCOME Br CI SO ₃ H Et Br CHO Me Br SO ₂ NHME Et Br SO ₃ H	Et	Me	Ph	OiPr	Me COMe
nBu nPr Et SiPr Me CONHMe tBu nBu iPr NH2 Et CONHMs OMe H H NHMe Et NHMS OEt Me H NHEt Et NHCOME OiPr Et H NHPh Et NO2 OPh iPr CH2OH Me iPr CHO SET H CH2NH2 Et iPr SO3H SiPr Me CH2NHMe iPr iPr SO2NHME NH2 H CH2Ph H iPr OH NHME Me CH2CH2Ph H NHMS CI NHET Ph COME H NHCOME CI NHPh H COOH H NO2 CI CI Me CONH2 H CHO Br CI Et CONHME H SO3H Br CI Ph CONHMS ME SO2NHME Br Me CI NHMS ME OH Br Et CI NHCOME ME CI NHMS Ph CI NHCOME ME CI NHMS Ph CI NO2 ME CI NHCOME Br Me CHO Et CI NHCOME Br Me CHO Et CI NO2 Me Br CI SO3H ET BR CHO Me Br SO2NHME ET BR SO3H	iPr	Et	Н	Ph	Me COOH
tBu nBu iPr NH2 Et CONHMS OMe H H H NHMe Et NHMS OEt Me H NHEt Et NHCOME OiPr Et H NHPh Et NO2 OPh iPr CH2OH Me iPr CHO SEt H CH2NH2 Et iPr SO3H SiPr Me CH2NHMe iPr iPr SO2NHME NH2 H CH2Ph H iPr OH NHME ME CH2CH2Ph H NHMS CI NHET Ph COME H NHCOME CI NHPh H COOH H NO2 CI CI ME CONH2 H CHO Br CI Et CONHME H SO3H Br CI Ph CONHMS ME SO2NHME Br Me CI NHMS ME OH Br Et CI NHCOME ME CI NHMS Ph CI NHCOME ME CI NHMS Ph CI NHCOME ME CI NHCOME Br Me CHO Et CI NHCOME Br Me CHO Et CI NO2 Br CI SO3H ET Br SO3H	nPr	iPr	Me	SEt	Me CONH ₂
OMe H H NHMe Et NHMs OEt Me H NHEt Et NHCOME OiPr Et H NHPh Et NO2 OPh iPr CH2OH Me iPr CHO SEt H CH2NH2 Et iPr SO3H SiPr Me CH2NHME iPr iPr SO2NHME NH2 H CH2Ph H iPr OH NHME ME CH2CH2Ph H NHMS CI NHET Ph COME H NHCOME CI NHPh H COOH H NO2 CI CI ME CONH2 H CHO Br CI Et CONHME H SO3H Br CI Ph COMHMS ME SO2NHME Br ME CI NHCOME ME CI NHMS ME CI NHMS ME OH Br Et CI NHCOME ME CI NHCOME Br ME CHO Et CI NHCOME Br CHO Et CHO ME Br CHO ME Br SO2NHME ET Br SO3H	nBu	nPr	Et	SiPr	Me CONHMe
OEt Me OiPr Et H NHPh DiPr CH2OH Me OiPr Et H NHPh Et NO2 OPh iPr CH2OH Me SEt H CH2NH2 Et iPr SO3H SiPr Me NH2 H CH2Ph H iPr OH NHME ME NH4 H CH2Ph H NHMS CI NHET Ph COME H NHCOME CI NHPH H COOH H NO2 CI ME CONH2 H CHO Br CI Et CONHME H SO3H Br CI Ph COME H SO2NHME Br ME CI NHMS ME CI NHMS ME CI NHMS ME CI NHMS ME CI Ph CONHMS ME CI NHMS ME CI NHMS CI NHCOME CI NHCOM	tBu	nBu	iPr	NH_2	Et CONHMs
OiPr Et H NHPh Et NO2 OPh iPr CH2OH Me iPr CHO SEt H CH2NH2 Et iPr SO3H SiPr Me CH2NHMe iPr iPr SO2NHMe NH2 H CH2Ph H iPr OH NHME ME CH2CH2Ph H NHMS CI NHEt Ph COME H NHCOME CI NHPh H COOH H NO2 CI CI ME CONH2 H CHO Br CI Et CONHME H SO3H Br CI Ph CONHMS ME SO2NHME Br ME CI NHMS ME OH Br Et CI NHCOME ME CI NHMS Ph CI NO2 ME CI NHMS Ph CI NO2 ME CI NHCOME Br Me CHO Et CI NO2 Br CHO Et Br CHO ME Br SO3H Et Br CHO ME Br SO3H	OMe	Н	Н	NHMe	Et NHMs
OPh iPr CH2OH Me iPr CHO SEt H CH2NH2 Et iPr SO3H SiPr Me CH2NHMe iPr iPr SO2NHMe NH2 H CH2Ph H iPr OH NHME ME CH2CH2Ph H NHMS CI NHET Ph COME H NHCOME CI NHPh H COOH H NO2 CI CI ME CONH2 H CHO Br CI ET CONHME H SO3H Br CI Ph CONHMS ME SO2NHME Br ME CI NHCOME ME CI NHMS ME CI NHMS ME CI NHMS Ph CI NHCOME ME CI NHMS Ph CI NHCOME ME CI NHCOME Br Me CHO ET CI NHCOME Br CHO ET Br CHO ME Br SO3H ET BR SO3H	OEt	Me	Н	NHEt	Et NHCOMe
SEt H SiPr Me CH ₂ NHMe IPr IPr SO ₃ H SiPr Me CH ₂ Ph H CH ₂ Ph H IPr OH NHMe Me CH ₂ CH ₂ Ph H NHMs CI NHEt Ph COMe H NHCOMe CI NHPh H COOH H NO ₂ CI CI Me CONH ₂ H CHO Br CI Et CONHMe H SO ₃ H Br CI Ph CONHMS Me SO ₂ NHMe Br Me CI NHCOMe Me CI NHMS Me CI NHCOME Br Me CHO Et CHO Et CHO Br CH BR CHO BR CH BR CHO BR CH	OiPr	Et	Н	NHPh	Et NO ₂
SiPr Me CH ₂ NHMe iPr iPr SO ₂ NHMe NH ₂ H CH ₂ Ph H iPr OH NHMe Me CH ₂ CH ₂ Ph H NHMs CI NHEt Ph COMe H NHCOME CI NHPh H COOH H NO ₂ CI CI Me CONH ₂ H CHO Br CI Et CONHME H SO ₃ H Br CI Ph CONHMS ME SO ₂ NHME Br Me CI NHMS ME OH Br Et CI NHCOME ME CI NHMS Ph CI NHCOME ME CI NHMS Ph CI SO ₃ H Et Br CHO ME Br SO ₂ NHME Et Br SO ₃ H	OPh	iPr	CH ₂ OH	Me	iÞr CHO
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	SEt	Н	CH ₂ NH2	Et	iPr SO₃H
NHMe Me CH ₂ CH ₂ Ph H NHMs CI NHEt Ph COMe H NHCOMe CI NHPh H COOH H NO ₂ CI CI Me CONH ₂ H CHO Br CI Et CONHME H SO ₃ H Br CI Ph CONHMS Me SO ₂ NHMe Br Me CI NHCOME Me CI NHMS Ph CI NHCOME Me CI NHMS Ph CI NHCOME ME CI NHCOME Br Me CHO Et CI NHCOME Br CI SO ₃ H Et Br CHO Me Br SO ₂ NHME Et Br SO ₃ H	SiPr	Me	CH ₂ NHMe	iPr	iPr SO ₂ NHMe
NHEt Ph COMe H NHCOMe CI NHPh H COOH H NO2 CI CI Me CONH2 H CHO Br CI Et CONHME H SO3H Br CI Ph CONHMS ME SO2NHME Br ME CI NHMS ME OH Br Et CI NHCOME ME CI NHMS Ph CI NO2 ME CI NHCOME Br Me CHO Et CI NO2 Br CI SO3H Et Br CHO ME Br SO2NHME ET BR SO3H	NH_2	H	CH ₂ Ph	Н	iPr OH
NHPh H COOH H NO2 CI CI Me CONH2 H CHO Br CI Et CONHME H SO3H Br CI Ph CONHMS ME SO2NHME Br Me CI NHMS ME OH Br Et CI NHCOME ME CI NHMS Ph CI NO2 ME CI NHCOME Br Me CHO Et CI NO2 Br CI SO3H Et Br CHO Me Br SO2NHME Et Br SO3H	NHMe	Me	CH ₂ CH ₂ Ph	Н	NHMs CI
CI Me $CONH_2$ H CHO Br CI Et $CONHMe$ H SO_3H Br CI Ph $CONHMs$ Me SO_2NHMe Br CI NHMs Me CI NHMs Me CI NHMs Me CI NHMs CI NHMs CI NHMs CI NHMs CI NHMs CI NHMs CI NHCOMe CI NO2 CI NHCOMe CI NO3 H CI CI NO4 CI NO5 CI NO5 CI NO6 CI NHCOME CI NO6 CI NHCOME CI NO6 CI NHCOME CI NO6 CI NO6 CI NO7 CI NO6 CI NHCOME	NHEt	Ph	COMe	Н	NHCOMe CI
CI Et CONHMe H SO ₃ H Br CI Ph CONHMS Me SO ₂ NHMe Br Me CI NHMS Me OH Br Et CI NHCOME ME CI NHMS Ph CI NO ₂ Me CI NHCOME Br Me CHO Et CI NO ₂ Br CI SO ₃ H Et Br CHO Me Br SO ₂ NHMe Et Br SO ₃ H	NHPh	Н	COOH	Н	NO ₂ CI
CI Ph CONHMS Me SO ₂ NHMe Br Me CI NHMS Me OH Br Et CI NHCOME Me CI NHMS Ph CI NO ₂ Me CI NHCOME Br Me CHO Et CI NO ₂ Br CI SO ₃ H Et Br CHO Me Br SO ₂ NHMe Et Br SO ₃ H	Cl	Ме	CONH ₂	Н	CHO Br
Me CI NHMs Me OH Br Et CI NHCOMe Me CI NHMs Ph CI NO ₂ Me CI NHCOMe Br Me CHO Et CI NO ₂ Br CI SO ₃ H Et Br CHO Me Br SO ₂ NHMe Et Br SO ₃ H	CI	Et	CONHMe	Н	SO₃H Br
Et CI NHCOMe Me CI NHMs Ph CI NO ₂ Me CI NHCOMe Br Me CHO Et CI NO ₂ Br CI SO ₃ H Et Br CHO Me Br SO ₂ NHMe Et Br SO ₃ H	CI	Ph	CONHMs	Me	SO ₂ NHMe Br
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Me	CI	NHMs	Me	OH Br
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Et	Cl	NHCOMe	Me	CI NHMs
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Ph	CI	NO_2	Me	CI NHCOMe
Me Br SO_2NHMe Et Br SO_3H	· Br	Ме	CHO	Et	-
	Br	Cl	SO₃H	Et	Br CHO
CI Br OH Et Br SO ₂ NHMe	Me	Br	SO ₂ NHMe	Et	Br SO₃H
	CI	Br	OH	Et	Br SO ₂ NHMe

R ¹³ R ¹⁴	R ¹³	R ¹⁴	R ¹³ R ¹⁴
Me Et	H	ОН	H CH ₂ OH
Me iPr	Н	OMe	H CH ₂ NH2
Me nPr	Me	OEt	H CH ₂ NHMe
Me nBu	Et	OCF ₃	H CH ₂ Ph
Me tBu	iPr	OnPr	Me CH ₂ CH ₂ Ph
Et Me	Ph	OiPr	Me COMe
iPr Et	Н	Ph	Me COOH
nPr iPr	Me	SEt	Me CONH ₂
nBu nPr	Et	SiPr	Me CONHMe
tBu nBu	iPr	NH_2	Et CONHMs
OMe H	Н	NHMe	Et NHMs
OEt Me	Н	NHEt	Et NHCOMe
OiPr Et	Н	NHPh	Et NO ₂
OPh iPr	CH ₂ Ol	н Ме	iPr CHO
SEt H	CH ₂ NH		iPr SO₃H
SiPr Me	CH ₂ NHI	Ле iPr	iPr SO₂NHMe
NH_2 H	CH ₂ Pł	n H	iPr OH
NHMe Me	CH ₂ CH ₂	Ph H	NHMs Cl
NHEt Ph	COMe		NHCOMe CI
NHPh H	COOH	i H	NO ₂ CI
CI Me	CONH	₂ H	CHO Br
CI Et	CONHI	Ле Н	SO₃H Br
CI Ph	CONHI	/Is Me	SO ₂ NHMe Br
Me Cl	NHMs	s Me	OH Br
Et Cl	NHCON	/le Me	CI NHMs
Ph Cl	NO_2	Me	CI NHCOMe
· Br Me	CHO	Et	Cl NO ₂
Br Cl	SO ₃ H	Et	Br CHO
Me Br	SO ₂ NHI	•	Br SO₃H
CI Br	OH	Et	Br SO ₂ NHMe

R ¹¹	R ¹³	R ¹¹	R ¹³		R ¹¹	R ¹³
Н	Et	Н	CI		Н	OMe
Н	iPr	H	Br		Н	OCF ₃
Н	nPr	Н	NO_2		Н	OEt
Н	nBu	Н	CHO		Н	OiPr
Н	tBu	Н	SO₃H		Н	SMe
Me .	Н	Me	CI		Me	OMe
Me	Me	Me	Br		Me	OCF ₃
Me	Et	Me	CH ₂ OH		Me	OEt
Me	iPr	Me	CH_2NH_2		Me	SMe
Me	nPr	Me	CH ₂ NHMe		Me	OiPr
Me	nBu	Me	CH ₂ Ph		Me	OnPr
Et	Н	Et	COMe		Et	NHMe
Et	Me	Et	COOH		Et	NHEt
Et	Et	Et	CONH ₂		Et	NMe ₂
iPr	Н	iPr	CONHMe		iPr	NMeEt
nPr	Me	nPr	CONHMs		nPr	OMe
nBu	Et	nBu	NHMs		nBu	OCF ₃
tBu	Ме	tBu	NHCOMe		tBu	OEt
Ph	Ph	Ph	NO_2		Ph	OiPr
CH ₂ OH	Н	CH ₂ OH	CHO		CH ₂ OH	SMe
CH ₂ OH	Ме	CH ₂ OH	SO₃H		CH ₂ OH	OPh
CH ₂ OMe	Et	CH ₂ OMe	SO ₂ NHMe		CH ₂ OMe	SPh
CH ₂ OMe	Ph	CH ₂ OMe	ОН		CH ₂ OMe	NHPh
CH_2NH_2	Н	CH_2NH_2	COMe		CH ₂ NH ₂	OMe
CH ₂ NH ₂	Ме	CH_2NH_2	COOH		CH ₂ NH ₂	OCF ₃
CH ₂ NH ₂	Et	CH_2NH_2	CONH ₂		CH ₂ NH ₂	OEt
CH ₂ NHMe	Ме	CH ₂ NHMe	CONHMe		CH ₂ NHMe	OiPr
⊂ CH₂Ph	Ме	CH ₂ Ph	CONHMs		CH ₂ Ph	SMe
CH ₂ Ph	Et	CH ₂ Ph	NHMs		CH ₂ Ph	OPh
CH ₂ CH ₂ Ph	iPr	CH ₂ CH ₂ Ph	NO ₂	_	CH ₂ CH ₂ Ph	SPh

			141		
R ¹¹	R ¹³	R ¹¹	R ¹³	R ¹¹	R ¹³
Н	Et	Н	CI	Н	OMe
Н	iPr	Н	Br	Н	OCF ₃
Н	nPr	H	NO_2	Н	OEt
Н	nBu	H	CHO	Н	OiPr
Н	tBu	Н	SO₃H	Н	SMe
Me ·	Н	Me	CI	Me	OMe
Me	Ме	Me	Br	Me	OCF ₃
Me	Et	Me	CH ₂ OH	Me	OEt
Me	iPr	Me	CH ₂ NH ₂	Me	SMe
Me	nPr	Me	CH ₂ NHMe	Me	OiPr
Me	nBu	Me	CH ₂ Ph	Me	OnPr
Et	Н	Et	COMe	Et	NHMe
Et	Ме	Et	COOH	Et	NHEt
Et	Et	Et	CONH ₂	Et	NMe_2
iPr	Н	iPr	CONHMe	iPr	NMeEt
nPr	Me	nPr	CONHMs	nPr	OMe
nBu	Et	nBu	NHMs	nBu	OCF ₃
tBu	Ме	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO_2	Ph	OiPr
CH ₂ OH	H	CH ₂ OH	CHO	CH ₂ OH	SMe
CH ₂ OH	Ме	CH ₂ OH	SO₃H	CH ₂ OH	OPh
CH ₂ OMe	Et	CH ₂ OMe	SO ₂ NHMe	CH ₂ OMe	SPh
CH ₂ OMe	Ph	CH ₂ OMe	ОН	CH ₂ OMe	NHPh
CH ₂ NH ₂	Н	CH ₂ NH ₂	COMe	CH_2NH_2	OMe
CH ₂ NH ₂	Me	CH ₂ NH ₂	COOH	CH_2NH_2	OCF ₃
CH ₂ NH ₂	Et	CH ₂ NH ₂	CONH ₂	CH ₂ NH ₂	OEt
CH ₂ NHMe	Me	CH ₂ NHMe	CONHMe	CH ₂ NHMe	OiPr
CH ₂ Ph	Me	CH ₂ Ph	CONHMs	CH ₂ Ph	SMe
CH ₂ Ph	Et	CH ₂ Ph	NHMs	CH ₂ Ph	OPh
CH ₂ CH ₂ Ph	iPr	CH ₂ CH ₂ Ph	NO ₂	CH ₂ CH ₂ Ph	SPh

			TVIC			
R ¹¹	R ¹³	-	R ¹¹	R ¹³	R ¹¹	R ¹³
Н	Et		Н	CI	Н	OMe
Н	iPr		Н	Br	Н	OCF ₃
H.	nPr		Н	NO_2	Н	OEt
H	nBu		Н	CHO	Н	OiPr
Н	tBu		Н	SO₃H	Н	SMe
Me .	Н		Me	CI	Me	OMe
Ме	Ме		Ме	Br	Me	OCF ₃
Me	Et		Ме	CH ₂ OH	Me	OEt
Ме	iPr		Me	CH ₂ NH ₂	Ме	SMe
Me	nPr		Me	CH ₂ NHMe	Me	OiPr
Ме	nBu		Me	CH ₂ Ph	Ме	OnPr
Εt	Н		Et	COMe	Et	NHMe
Et	Me		Et	COOH	Et	NHEt
Εt	Et		Et	CONH ₂	Et	NMe ₂
iPr	Н		iPr	CONHMe	iPr	NMeEt
nPr	Me		nPr	CONHMs	nPr	OMe
nBu	Et	•	nBu	NHMs	nBu	OCF ₃
tBu	Me		tBu	NHCOMe	tBu	OEt
Ph	Ph		Ph	NO_2	Ph	OiPr
CH ₂ OH	Н		CH ₂ OH	CHO	CH ₂ OH	SMe
CH ₂ OH	Me		CH ₂ OH	SO₃H	CH ₂ OH	OPh
CH ₂ OMe	Et		CH ₂ OMe	SO ₂ NHMe	CH ₂ OMe	SPh
CH ₂ OMe	Ph		CH ₂ OMe	ОН	CH ₂ OMe	NHPh
CH ₂ NH ₂	Н		CH ₂ NH ₂	COMe	CH ₂ NH ₂	OMe
CH ₂ NH ₂	Me		CH ₂ NH ₂	COOH	CH ₂ NH ₂	OCF ₃
CH ₂ NH ₂	Et		CH_2NH_2	CONH ₂	CH ₂ NH ₂	OEt
CH ₂ NHMe	Me		CH ₂ NHMe	CONHMe	CH ₂ NHMe	OiPr
CH ₂ Ph	Ме		CH ₂ Ph	CONHMs	CH ₂ Ph	SMe
CH ₂ Ph	Et		CH ₂ Ph	NHMs ·	CH ₂ Ph	OPh
CH ₂ CH ₂ Ph	iPr		CH ₂ CH ₂ Ph	NO ₂	CH ₂ CH ₂ Ph	SPh

R11 R13 R11 R13 R11 R13 H Et H CI H OMe H iPr H Br H OCF₃ H nPr H NO₂ H OEt H nBu H CHO H OiPr H tBu H CHO H OiPr Me H Me CH₂OH Me OEt Me Br Me OEt Me SMe Me iPr Me CH₂NHAe Me OiPr Me iPr Me CH₂NHAe Me OiPr Me iPr Me CH₂NHAe Me OiPr Me iPr <							
H	R ¹¹	R ¹³	R ¹¹	R ¹³		₹11	R ¹³
H iPr H Br H OCF₃ H nPr H NO₂ H OEt H nBu H CHO H OiPr H tBu H SO₃H H SMe Me H Me CI Me OMe Me Me Me Br Me OCF₃ Me iPr Me CH₂OH Me OEt Me iPr Me CH₂NHMe Me OiPr Me nBu Me CH₂Ph Me OnPr Et H Et COMe Et NHMe Et Me Et CONH₂ Et NMe₂ iPr H iPr CONHMs nPr OMe nBu Et Et COMe Bu NHMs nBu OCF₃ NMe DPr Me NMe CH₂NHMe Me OiPr Me NBu Me CH₂Ph Me OnPr Et H Et COMH₂ Et NHEt Et Et Et Et CONH₂ Et NMe₂ iPr H iPr CONHMs nPr OMe nBu Et nBu NHMs nBu OCF₃ tBu Me tBu NHMs nBu OCF₃ tBu Me TBu NHMS nBu OCF₃ tBu Me TBu NHCOME TBu OFt CH₂OH H CH₂OH CHO CH₂OH SMe CH₂OH Me CH₂OH SO₃H CH₂OH SPh CH₂OME Et CH₂OME SO₂NHME CH₂OME SPh CH₂NH₂ Et CH₂NH₂ COME CH₂NH₂ OME CH₂NH₂ Et CH₂NH₂ COME CH₂NH₂ Et CH₂NH₂ COME CH₂NH₂ Et CH₂NH₂ COME CH₂NH₂ Et CH₂NHB CONHMB CH₂NH₂ OEt CH₂NHB ME CH₂NHB CONHMB CH₂Ph SME CH₂Ph Me CH₂Ph NHMS CH₂Ph SME	Н	Et	H	Cl	-	H	OMe
H nBu H CHO H SMe Me H Me CI Me OMe Me Me Me Br Me OCF₃ Me Et Me CH₂OH Me OEt Me iPr Me CH₂NH₂ Me SMe Me nPr Me CH₂NHMe Me OiPr Me nBu Me CH₂Ph Me OnPr Et H Et COMe Et NHMe Et Et Et CONH₂ Et NMe₂ iPr H iPr CONHMe iPr NMeEt nPr Me nBu NHMs nBu OCF₃ tBu Me tBu NHCOMe tBu OEt NHMe nBu Me CH₂OH Et NHEt CH₂Ph Me CH₂OH OPh CH₂OH H CH₂OH OPh CH₂OH CH₂OME SO₂NHME CH₂OME SPh CH₂OH ME CH₂NH₂ COME CH₂OH CH₂OH OPH CH₂OH CH₂OH OPH CH₂OH CH₂OH OPH CH₂OH CH₂OH CHO CH₂OH SME CH₂OH ME CH₂OH OPH CH₂OH CH₂OME CH₂OME SPh CH₂OH ME CH₂OME OH CH₂OME SPh CH₂OH ME CH₂OME OH CH₂OME SPh CH₂OME Et CH₂OME OH CH₂OME NHPh CH₂NH₂ Et CH₂NH₂ COOH CH₂OH OME CH₂NH₂ Et CH₂NH₂ COOH CH₂NH₂ OGE CH₂NHAE CH₂Ph ME CH₂Ph SME CH₂Ph ME CH₂Ph CONHMS CH₂Ph SME CH₂Ph ME CH₂Ph NHMS CH₂Ph OPh	Н	iPr	Н	Br		Н	OCF ₃
H tBu H SO3H H SMe Me H Me CI Me OMe Me H Me CI Me OMe Me Me Me Br Me OCF3 Me Bet Me CH2OH Me OCF3 Me Et Me CH2NH2 Me SMe Me nPr Me CH2NHMe Me OIPr Me nPr Me CH2Ph Me OnPr Me nBu Me CH2Ph Me OnPr Et H Et COMe Et NHMe Et H Et COMe Et NHMe Et Et CONH2 Et NMe2 iPr H iPr CONHMe iPr NMeEt nPr ONHMe nPr OMe OCF3 tBu Me tBu	Н	nPr	Н			Н	OEt
Me H Me CI Me OMe Me Me Me Br Me OCF3 Me Et Me CH2OH Me OCF3 Me IPr Me CH2OH Me OCF3 Me IPr Me CH2NHMe Me OCF3 Me nPr Me CH2Ph Me OCF7 Me nBu Me CH2Ph Me OCF7 Me nBu Me CH2Ph Me OCF7 Et H Et COME Et NHMe Et Me Et COMH Et NHEt Et Et COMH IPr NMeEt NMe2 IPr NMeEt NMe OCF3 NMeEt NPr OMe NMe OCF3 NMe OCF3 NMe OCF3 NMe OCF3 NMe OCF3 NMe OCH3 DPh OMe OCH3 <td>Н</td> <td>nBu</td> <td>Н</td> <td>CHO</td> <td></td> <td>Н</td> <td>OiPr</td>	Н	nBu	Н	CHO		Н	OiPr
Me Me Me Br Me OCF3 Me Et Me CH2OH Me OEt Me IPr Me CH2NH2 Me SMe Me IPr Me CH2NHME Me OIPr Me nPr Me CH2Ph Me OIPr Me nBu Me CH2Ph Me OIPr Me nBu Me CH2Ph Me OIPr Me nBu Me CH2Ph Me OIPr Et H Et COMe Et NHMe Et NHMe Et NHMe IPr NMe2 IPr NMe2 IPr NMe2 IPr NMe2 IPr NMe2 IPr NMe2 IPr NMe3 NBU OCF3 SUM OCF3 SUM OCF3 SUM OCF3 SUM OCF3 SUM OCF3 OCF3 OCF3 OCF3 OCF3 OCF3	Н	tBu	Н	SO₃H		Н	SMe
Me Et Me CH ₂ OH Me OEt Me iPr Me CH ₂ NH ₂ Me SMe Me nPr Me CH ₂ NHMe Me OiPr Me nBu Me CH ₂ Ph Me OnPr Et H Et COMe Et NHMe Et Me Et COOH Et NHEt Et Et Et CONH ₂ Et NHMe iPr NMeEt nPr H iPr CONHMe iPr NMeEt nPr Me nBu NHMs nBu OCF ₃ tBu Me TBu NHCOMe tBu OEt Ph Ph Ph NO ₂ Ph OiPr CH ₂ OH H CH ₂ OH CH ₂ OH SMe CH ₂ OH CH ₂ OH SPh CH ₂ OH CH ₂ OMe CH ₂ OH Me CH ₂ OHMe CONHMe CH ₂ OHMe OiPr CH ₂ OH Me CH ₂ OHMe CONHME CH ₂ OHME OPh OPh CH ₂ OH Et CH ₂ OH NHMS CH ₂ Ph OPh OPh OPh CH ₂ OH Et CH ₂ OH NHMS CH ₂ Ph OPh OPh OPh OPh OPh OPh OPh OPh OPh O	Me	Н	Me	CI		Me	OMe
Me Et Me CH2OH Me OEt Me iPr Me CH2NH2 Me SMe Me nPr Me CH2NHMe Me OiPr Me nPr Me CH2Ph Me OiPr Me nBu Me CH2Ph Me OiPr Et H Et COMe Et NHMe Et H Et COOH Et NHMe Et H Et COOH Et NHEt Et Et COOH Et NHEt IPr H iPr CONHMe iPr NMeEt nPr OME nPr OME OME nBu Et nBu NHMs nBu OCF3 tBu Me tBu NHCH OH		Me	Me			Ме	OCF ₃
Me nPr Me nBu Me nBu Me CH ₂ NHMe Me OiPr Me nBu Me CH ₂ Ph Me OnPr Me nBu Me CH ₂ Ph Me OnPr Me Me OiPr Me Me OiPr Me Me OiPr Me Me OiPr Me Me Me OiPr Me		Et	Me	CH ₂ OH		Me	OEt
MenPrMeCH2NHMeMeOiPrMenBuMeCH2PhMeOnPrEtHEtCOMeEtNHMeEtHEtCOOHEtNHEtEtEtEtCOOHEtNHEtEtEtEtCONHMeiPrNMeEtiPrHiPrCONHMeiPrNMeEtnPrMenPrCONHMsnPrOMenBuEtnBuNHMsnBuOCF3tBuMetBuNHMsnBuOCF3tBuMetBuNHCOMetBuOEtPhPhPhNO2PhOiPrCH2OHHCH2OHCH0CH2OHSMeCH2OHHCH2OHSO3HCH2OHOPhCH2OMeEtCH2OMeSO2NHMeCH2OMeSPhCH2OMePhCH2OMeOHCH2OMeNHPhCH2NH2HCH2OMeOHCH2OMeNHPhCH2NH2MeCH2NH2COOHCH2NH2OEtCH2NH4EtCH2NH2CONHMeCH2NHMeOiPrCH2PhMeCH2PhCONHMsCH2PhSMeCH2PhEtCH2PhCNHMsCH2PhOPh		iPr	Me	CH ₂ NH ₂		Ме	SMe
Me nBu Me CH ₂ Ph Me OnPr Et H Et COMe Et NHMe Et Me Et COOH Et NHEt Et Et Et Et CONH ₂ Et NMe ₂ iPr H iPr CONHMe iPr NMeEt nPr Me nPr CONHMs nPr OMe nBu Et nBu NHMs nBu OCF ₃ tBu Me tBu NHCOMe tBu OEt Ph Ph Ph NO ₂ Ph OiPr CH ₂ OH H CH ₂ OH CHO CH ₂ OH SMe CH ₂ OH Me CH ₂ OH SO ₃ H CH ₂ OH OPh CH ₂ OMe Et CH ₂ OMe SO ₂ NHMe CH ₂ OMe SPh CH ₂ OMe Ph CH ₂ OMe OH CH ₂ OMe SPh CH ₂ NH ₂ H CH ₂ NH ₂ COMe CH ₂ NH ₂ OMe CH ₂ NH ₂ Me CH ₂ NH ₂ COOH CH ₂ NH ₂ OCF ₃ CH ₂ NH ₂ Et CH ₂ NH ₂ CONH ₂ CH ₂ NH ₂ OEt CH ₂ NHMe Me CH ₂ Ph CONHMS CH ₂ Ph SMe CH ₂ Ph Et CH ₂ Ph NHMS CH ₂ Ph OPh		nPr	Me	CH ₂ NHMe		Ме	OiPr
Et H Et COMe Et NHMe Et Me Et COOH Et NHEt Et Et Et CONH2 Et NMe2 iPr H iPr CONHME iPr NMeEt nPr Me nPr CONHMS nPr OMe nBu Et nBu NHMS nBu OCF3 tBu Me tBu NHCOMe tBu OEt Ph Ph Ph NO2 Ph OiPr CH2OH H CH2OH SO3H CH2OH OPh CH2OME Et CH2OME SO2NHME CH2OME SPh CH2OME Ph CH2OME OH CH2OME NHPh CH2NH2 H CH2NH2 COOH CH2NH2 OME CH2NH2 Et CH2NH2 COOH CH2NH2 OME CH2NH4 CH2NH2 CONHME CH2NH2 OEt CH2NHME ME CH2Ph ME CH2Ph SME CH2Ph ME CH2Ph NHMS CH2Ph SME		nBu	Me	CH ₂ Ph		Ме	OnPr
Et Me Et COOH Et NHEt Et Et CONH2 Et NHEt Et Et CONH2 Et NMe2 iPr H iPr CONHME iPr NMeEt nPr Me nPr CONHMS nPr OME nBu Et nBu NHMS nBu OCF3 tBu Me tBu NHCOME tBu OEt Ph Ph Ph Ph NO2 Ph OiPr CH2OH H CH2OH CH2OH SO3H CH2OH OPh CH2OME Et CH2OME SO2NHME CH2OME SPh CH2OME Ph CH2OME OH CH2OME NHPh CH2NH2 H CH2NH2 COOH CH2OME NHPh CH2NH2 H CH2NH2 COOH CH2OME NHPh CH2NH2 Et CH2NH2 COOH CH2NH2 OME CH2NH2 OCF3 CH2NHME ME CH2NH4 CONHME CH2NH4 OET CH2NHME ME CH2Ph ME CH2Ph SME CH2PH		Н	Et	COMe		Et	NHMe
iPr H iPr CONHMe iPr NMeEt nPr Me nPr CONHMs nPr OMe nBu Et nBu NHMs nBu OCF3 tBu Me tBu NHCOMe tBu OEt Ph Ph Ph NO2 Ph OiPr CH2OH H CH2OH CHO CH2OH SMe CH2OH Me CH2OH SO3H CH2OH OPh CH2OME Et CH2OME SO2NHME CH2OME SPh CH2OME Ph CH2OME OH CH2OME NHPh CH2NH2 H CH2NH2 COME CH2NH2 OME CH2NH2 ME CH2NH2 COOH CH2NH2 OME CH2NH2 Et CH2NH2 COOH CH2NH2 OEt CH2NHME ME CH2NHME CONHME CH2NH2 OEt CH2NHME ME CH2NHME CONHME CH2NHME OiPr CH2Ph ME CH2Ph NHMS CH2Ph SME CH2Ph SME		Ме	Et	COOH		Et	NHEt
iPr H iPr CONHMe iPr NMeEt nPr Me nPr CONHMs nPr OMe nBu Et nBu NHMs nBu OCF3 tBu Me tBu NHCOMe tBu OEt Ph Ph Ph Ph NO2 Ph OiPr CH2OH H CH2OH SO3H CH2OH OPh CH2OMe Et CH2OMe SO2NHMe CH2OMe SPh CH2OMe Ph CH2OMe OH CH2OMe SPh CH2OMe Ph CH2OMe OH CH2OMe NHPh CH2NH2 H CH2NH2 COME CH2NH2 OME CH2NH2 OME CH2NH2 DME CH2NH2 Et CH2NH2 COOH CH2NH2 OEt CH2NH2 Et CH2NH2 CONH2 CH2NH2 OEt CH2NHME ME CH2NHME CONHME CH2NHME OIPr CH2Ph Me CH2Ph NHMS CH2Ph SME CH2Ph SME CH2Ph SME CH2Ph OPh	Et	Et	Et	CONH ₂		Et	NMe_2
nBu Et nBu NHMs nBu OCF3 tBu Me tBu NHCOMe tBu OEt Ph Ph Ph NO2 Ph OiPr CH2OH H CH2OH CHO CH2OH SMe CH2OH ME CH2OH SO3H CH2OH OPh CH2OME Et CH2OME SO2NHME CH2OME SPh CH2OME Ph CH2OME OH CH2OME NHPh CH2NH2 H CH2NH2 COME CH2NH2 OME CH2NH2 ME CH2NH2 COOH CH2NH2 OCF3 CH2NH2 Et CH2NH2 COOH CH2NH2 OEt CH2NHME ME CH2NHME CONHME CH2NHME OiPr CH2Ph ME CH2Ph NHMS CH2Ph OPh		Н	iPr	CONHMe		iPr	NMeEt
The state of the s	nPr	Ме	nPr	CONHMs		nPr	OMe
tBu Me tBu NHCOMe tBu OEt Ph Ph Ph NO2 Ph OiPr CH2OH H CH2OH CHO CH2OH SMe CH2OH Me CH2OH SO3H CH2OH OPh CH2OMe Et CH2OME SO2NHME CH2OME SPh CH2OME Ph CH2OME OH CH2OME NHPh CH2NH2 H CH2NH2 COME CH2NH2 OME CH2NH2 ME CH2NH2 COOH CH2NH2 OCF3 CH2NH2 Et CH2NH2 CONH2 CH2NH2 OEt CH2NHME ME CH2NHME CONHME CH2NHME OiPr CH2Ph ME CH2Ph NHMS CH2Ph SME CH2Ph SME		Et	• nBu	NHMs	i	nBu	OCF ₃
CH ₂ OH H CH ₂ OH CHO CH ₂ OH SMe CH ₂ OH Me CH ₂ OH SO ₃ H CH ₂ OH OPh CH ₂ OMe Et CH ₂ OMe SO ₂ NHMe CH ₂ OMe SPh CH ₂ OMe Ph CH ₂ OMe OH CH ₂ OMe NHPh CH ₂ NH ₂ H CH ₂ NH ₂ COMe CH ₂ NH ₂ OMe CH ₂ NH ₂ Me CH ₂ NH ₂ COOH CH ₂ NH ₂ OCF ₃ CH ₂ NH ₂ Et CH ₂ NH ₂ CONH ₂ CH ₂ NH ₂ OEt CH ₂ NHMe Me CH ₂ NHMe CONHMe CH ₂ NHMe OiPr CH ₂ Ph Me CH ₂ Ph CONHMs CH ₂ Ph SMe CH ₂ Ph Et CH ₂ Ph NHMs CH ₂ Ph OPh	tBu	Me	tBu	NHCOMe		tBu	OEt
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Ph	Ph	Ph	NO_2		Ph	OiPr
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Н	CH ₂ OH	CHO	CI	H ₂ OH	SMe
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Ме	CH ₂ OH	SO₃H	C	H_2OH	OPh
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	_	Et	CH ₂ OMe	SO ₂ NHMe	CH	l ₂ OMe	SPh
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	_	Ph	CH ₂ OMe	ОН	CH	l ₂ OMe	NHPh
CH_2NH_2 Me CH_2NH_2 COOH CH_2NH_2 OCF ₃ CH_2NH_2 Et CH_2NH_2 CONH ₂ CH_2NH_2 OEt CH_2NHMe Me CH_2NHMe CONHMe CH_2NHMe OiPr CH_2Ph Me CH_2Ph CONHMs CH_2Ph SMe CH_2Ph Et CH_2Ph NHMs CH_2Ph OPh		Н	CH_2NH_2	COMe	Ch	H_2NH_2	OMe
CH_2NH_2 Et CH_2NH_2 $CONH_2$ CH_2NH_2 OEt CH_2NHMe Me CH_2NHMe $CONHMe$ CH_2NHMe OiPr CH_2Ph Me CH_2Ph $CONHMs$ CH_2Ph SMe CH_2Ph Et CH_2Ph $NHMs$ CH_2Ph OPh		Me	CH_2NH_2	COOH	CH	H_2NH_2	OCF ₃
CH_2NHMe Me CH_2NHMe $CONHMe$ CH_2NHMe $OiPr$ CH_2Ph Me CH_2Ph $CONHMs$ CH_2Ph CH_2P		Et	CH_2NH_2	CONH ₂	Cl	H_2NH_2	OEt
CH_2 Ph Me CH_2 Ph CONHMs CH_2 Ph SMe CH_2 Ph Et CH_2 Ph NHMs CH_2 Ph OPh		Ме	CH ₂ NHMe		CH	₂ NHMe	OiPr
CH ₂ Ph Et CH ₂ Ph NHMs CH ₂ Ph OPh	-	Ме	CH ₂ Ph	CONHMs	С	H ₂ Ph	SMe
T ' OLI OLI DL. NO ' OLI OLI DL. ODL	-		CH ₂ Ph	NHMs	С	H ₂ Ph	OPh
CH ₂ CH ₂ Ph iPr CH ₂ CH ₂ Ph NO ₂ CH ₂ CH ₂ Ph SPh	_ ,	iPr	CH ₂ CH ₂ Ph	NO ₂	CH ₂	₂ CH ₂ Ph	SPh

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R ¹¹	R ¹³	R ¹¹	R ¹³	R ¹¹	R ¹³
Н	Et	Н	CI	Н	OMe
Н	iPr	Н	Br	Н	OCF ₃
Н	nPr	Н	NO_2	Н	OEt
Н	nBu	Н	CHO .	Н	OiPr
Н	tBu	Н	SO₃H	Н	SMe
Me	Н	Me	CI	Me	OMe
Me	Ме	Me	Br	Me	OCF ₃
Me	Et	Me	CH ₂ OH	Me	OEt
Me	iPr	Me	CH ₂ NH ₂	Me	SMe
Me	nPr	Me	CH ₂ NHMe	Me	OiPr
Me	nBu	Me	CH ₂ Ph	Ме	OnPr
Et	Н	Et	COMe	Et	NHMe
Et	Ме	Et	COOH	Et	NHEt
Et	Et	Et	CONH ₂	Et	NMe ₂
iPr	Н	iPr	CONHMe	iPr	NMeEt
nPr	Ме	nPr	CONHMs	['] nPr	OMe
nBu	Et	nBu	NHMs	nBu	OCF ₃
tBu	Me	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO_2	Ph	OiPr
CH ₂ OH	Н	CH ₂ OH	CHO	CH ₂ OH	SMe
CH ₂ OH	Me	CH ₂ OH	SO₃H	CH ₂ OH	OPh
CH ₂ OMe	Et	CH ₂ OMe	SO ₂ NHMe	CH ₂ OMe	SPh
CH ₂ OMe	Ph	CH ₂ OMe	ОН	CH ₂ OMe	NHPh
CH ₂ NH ₂	H	CH ₂ NH ₂	COMe	CH_2NH_2	OMe
CH ₂ NH ₂	Me	CH ₂ NH ₂	COOH	CH_2NH_2	OCF ₃
CH_2NH_2	Et	CH ₂ NH ₂	CONH ₂	CH_2NH_2	OEt
CH ₂ NHMe	Ме	CH ₂ NHMe	CONHMe	CH ₂ NHMe	OiPr
CH ₂ Ph.	Me	CH ₂ Ph	CONHMs	CH ₂ Ph	SMe
CH ₂ Ph	Et	$\mathrm{CH_2Ph}$	NHMs	CH ₂ Ph	OPh
CH ₂ CH ₂ Ph	iPr	CH ₂ CH ₂ Ph	NO ₂	CH ₂ CH ₂ Ph	SPh

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R ¹¹	R ¹³	R ¹¹	R ¹³	R ¹¹	R ¹³
Н	Et	Н	Cl	Н	OMe
H	iPr	Н	Br	Н	OCF ₃
H	nPr	Н	NO_2	Н	OEt
 Н	nBu	Н	CHO	Н	OiPr
H	tBu	Н	SO₃H	Н	SMe
Me	Н	Me	CI	Me	OMe
Me	Me	Ме	Br	Me	OCF ₃
Me	Et	Me	CH ₂ OH	Me	OEt
Me	iPr	Me	CH ₂ NH ₂	Ме	SMe
Me	nPr	Me	CH ₂ NHMe	Me	OiPr
Me	nBu	Me	CH ₂ Ph	Me	OnPr
Et ·	Н	Et	COMe	Et	NHMe
Et	Me	Et	COOH	Et	NHEt
Et	Et	Et	CONH ₂	Et	NMe_2
iPr	H	iPr	CONHMe	iPr	NMeEt
nPr	Ме	nPr	CONHMs	nPr	OMe
nBu	Et	nBu	NHMs	nBu	OCF ₃
tBu	Me	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO_2	Ph	OiPr
CH ₂ OH	Н	CH ₂ OH	CHO	CH ₂ OH	SMe
CH ₂ OH	Me	CH ₂ OH	SO₃H	CH ₂ OH	OPh
CH ₂ OMe	Et	CH ₂ OMe	SO ₂ NHMe	CH ₂ OMe	SPh
CH ₂ OMe	Ph	CH ₂ OMe	ОН	CH ₂ OMe	NHPh
CH ₂ NH ₂	Н	CH ₂ NH ₂	COMe	CH_2NH_2	OMe
CH ₂ NH ₂	Me	CH ₂ NH ₂	COOH	CH_2NH_2	OCF ₃
CH ₂ NH ₂	Et	CH ₂ NH ₂	CONH ₂	CH ₂ NH ₂	OEt
CH ₂ NHMe	Me	CH ₂ NHMe	CONHMe	CH ₂ NHMe	OiPr
CH ₂ Ph .	Me	CH ₂ Ph	CONHMs	CH₂Ph	SMe
CH ₂ Ph	Et	CH ₂ Ph	NHMs	CH ₂ Ph	OPh
CH ₂ CH ₂ Ph	iPr	CH ₂ CH ₂ Ph	NO ₂	CH ₂ CH ₂ Ph	SPh

R ¹¹	R ¹³	R ¹¹	R ¹³	R ¹¹	R ¹³
Н	Et	Н	CI	Н	OMe
H	iPr	Н	Br	Н	OCF ₃
H	nPr	Н	NO ₂	Н	OEt
H	nBu	Н	CHO	Н	OiPr
H	tBu	Н	SO₃H	Н	SMe
Me	Н	Ме	Cl	Me	OMe
Me	Me	Ме	Br	Me	OCF ₃
Me	Et	Ме	CH ₂ OH	Me	OEt
Me	iPr	Me	CH ₂ NH ₂	Me	SMe
Me	nPr	Ме	CH ₂ NHMe	Me	OiPr
Me	nBu	Me	CH ₂ Ph	Me	OnPr
Et	Н	Et	COMe	Et	NHMe
Et	Ме	Et	COOH	Et	NHEt
Et	Et	Et	CONH ₂	Et	NMe ₂
iPr	Н	iPr	CONHMe	iPr	NMeEt
nPr	Ме	nPr	CONHMs	nPr	ОМе
nBu	Et	nBu	NHMs	nBu	OCF ₃
tBu	Ме	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO_2	Ph	OiPr
CH ₂ OH	Н	CH ₂ OH	CHO	CH ₂ OH	SMe
CH ₂ OH	Me	CH ₂ OH	SO₃H	CH ₂ OH	OPh
CH ₂ OMe	Et	CH ₂ OMe	SO ₂ NHMe	CH ₂ OMe	SPh
CH ₂ OMe	Ph	CH ₂ OMe	ОН	CH ₂ OMe	NHPh
CH_2NH_2	Н	CH_2NH_2	COMe	CH_2NH_2	OMe
CH_2NH_2	Me	CH ₂ NH ₂	COOH	CH ₂ NH ₂	OCF ₃
CH ₂ NH ₂	Et	CH ₂ NH ₂	CONH ₂	CH ₂ NH ₂	OEt
CH ₂ NHMe	Me	CH ₂ NHMe	CONHMe	CH ₂ NHMe	OiPr
CH₂Ph.	Me	CH ₂ Ph	CONHMs	CH ₂ Ph	SMe
CH ₂ Ph	Et	CH ₂ Ph	NHMs	CH ₂ Ph	OPh
CH ₂ CH ₂ Ph	iPr	CH ₂ CH ₂ Ph	NO ₂	CH ₂ CH ₂ Ph	SPh

R ¹¹	R ¹³	R ¹¹	R ¹³	R ¹¹	R ¹³
Н	Et	H	Cl	Н	OMe
H	iPr	Н	Br	Н	OCF ₃
H	nPr	Н	NO_2	Н	OEt
	nBu	Н	CHO	Н	OiPr
H	tBu	Н	SO₃H	Н	SMe
Me	Н	Me	Cl-	Me	OMe
Me	Me	Me	Br	Me	OCF ₃
Me	Et	Me	CH ₂ OH	Me	OEt
Me	iPr	Me	CH ₂ NH ₂	Me	SMe
Me	nPr	Me	CH ₂ NHMe	Me	OiPr
Me	nBu	Me	CH ₂ Ph	Me	OnPr
Et	Н	Et	COMe	Et	NHMe
Et	Me	Εt	COOH	Et	NHEt
Et	Et	Et	CONH ₂	Et	NMe_2
iPr	Н	iPr	CONHMe	iPr	NMeEt
nPr	Me	nPr	CONHMs	nPr	OMe
nBu	Et	nBu	NHMs	nBu	OCF ₃
tBu	Me	tBu	NHCOMe	tBu	OEt
Ph	Ph	Ph	NO ₂ '	Ph	OiPr
CH ₂ OH	H	CH ₂ OH	CHO	CH ₂ OH	SMe
CH ₂ OH	Me	CH ₂ OH	SO₃H	CH ₂ OH	OPh
CH ₂ OMe	Et	CH ₂ OMe	SO ₂ NHMe	CH ₂ OMe	SPh
CH ₂ OMe	Ph	CH ₂ OMe	OH	CH ₂ OMe	NHPh
CH ₂ NH ₂	Н	CH ₂ NH ₂	COMe	CH_2NH_2	OMe
CH ₂ NH ₂	Ме	CH ₂ NH ₂	COOH	CH_2NH_2	OCF ₃
CH ₂ NH ₂	Et	CH ₂ NH ₂	CONH ₂	CH_2NH_2	OEt
CH ₂ NHMe	Me	CH ₂ NHMe	CONHMe	CH ₂ NHMe	OiPr
· CH ₂ Ph	Me	⊂ CH ₂ Ph	CONHMs	CH ₂ Ph	SMe
CH ₂ Ph	Et	CH ₂ Ph	NHMs	CH ₂ Ph	OPh
CH ₂ CH ₂ Ph	iPr	CH ₂ CH ₂ Ph	NO ₂	CH ₂ CH ₂ Ph	SPh ———

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HN-Me	HN	HN HN
HNEt	HN	HN HN
HN		ÓH ✓
HN	HN	HN
HN	HN	HN HN F
HN	HN	HN HN
HN /	HN	F Me
HN	,	HN HN
HN	HN	HN S HN
HN	HN	HN
HN	HN	HN O. HN
HN .	HN	$HN \longrightarrow N \longrightarrow HN \longrightarrow S \longrightarrow M$
HN OH	HN	HN O HN O
Ö		

HN-R

HN SO ₃ H	OMe	Me HN Me
H ₂ NO ₂ S	MeOCO	OMe
CH ₂ OH	NHCOOEt	HNOMe
HN COCH3	HN OPh	HN OMe
HN	OCOCH ₃	CO_2H NO_2
HN	Me OH HN	OMe
HN	OH Me	NHCOPh Br
HN .	OH Br	
HN	HN	HN H

HN	-R
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HNMe	HN	HN HN
HN-Et	HN	HN HN
HN		OH
HN	HN	HN HN
HN	HN	HN HN F
HN	HN	HN HN
HN	HN	F Me
HN		HN N
HN	HN	HN S HN
HN	HN	HN
HN	HN	HN O HN
HN	HN	$HN \longrightarrow N$ H $HN \longrightarrow S$
HN OH	HN	HN O HN O

HN-R

HN−R

HN-R

н	N	 R
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HN-Me	HN	HN HN	
HNEt	HN	HN OH HN	
HN			
HN	HN	HN	F
HN .	HN	HN O HN	F
HN	HN	HN. HN	
HN	HN	F Me	\bigcap
HN	,	HN N	
HN	HN	HN S	
HN	HN	HN O	
HN	HN	HN O HN	✓
HN	HN	HN N HN N	s
HN OH	HN	HN O HN	
O			

HN-R

HN-R

HN-R			
HN	HN	$HN \longrightarrow N \longrightarrow$	HN N
HN N-N	HN	HN NO	HN N
HN N	HN	HN	HN
HN N	HN N	HN	HŅ⟨ O
HN N CI	HN N CI	HN NH	HN
N	о N н	N	HN
HN N	HN N	FN	HN
HN	HN	HN N-S	Ö
HN	HN N	HN	HN
HN	HN	$-HN \longrightarrow N$	HN N

HN-Me	HN	HN HN
HN-Et	HN	HN HN
HN		ÓН
HN	HN	HN
HN	HN	HN O F
HN	HN	HN HN
HN	HN	HN HN HN
HN	HN	HN S HN
HN	HN	HN
HN	HN	HN HN
HN	HN	$HN \longrightarrow N \longrightarrow HN \longrightarrow S \longrightarrow M$
HN OH	HN	HN O HN O
Ö		

HN SO ₃ H	OMe	Me Me Me
H ₂ NO ₂ S	MeOCO	OMe
CH₂OH HN	NHCOOEt	HNOMe
COCH₃	OPh	HNOMe
CI	OCOCH ₃	HN NO ₂
HN	Me OH	OMe
6-/	OH Me	HN Br
HN	OH Br	HN H

HN-R

HN	HN	HN	HN N
HN N-N	HN	HN	HN
HN N	HN	HN	HN N
HN N	HN N	HN	<u>,</u>
HN N CI	HN CI	HN NH	HN
N	^	N O	HN
HN N	HN	. N	IN N
HN	HN	HN	HN O
HN	HN N H	HN N-S	HN
HN	HN	HN S	HN O H

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HN-Me	HN	HN HN
HN-Et	HN	HN OH HN
HN		
HN	HN	HN
HN	HN	HN HN F
HN	HN	HN
HN	HN	F Me
HN	····	HN HN N
HN	HN	HN S HN
HN	HN	HN
HN	HN	HN
HN	HN	$HN \longrightarrow N$ H $HN \longrightarrow S$
HNOH	HN	HN O HN O
HN	TIIN	· · · · · · · · · · · · · · · · · · ·

HN-R

HN-R

HN-R			
HN	HN	HN	N
HN N-N	HN	HN	HN
HN N=	HN	HN	HN N
HN N	HN	HN	HŅ
HN N CI	N CI	HN N NH	HN
N	N H		HN
HN	HN N	, _N	HN N
HN	HN	HN N-S	Ö
HN	HN N	HN N-S	HN
HN	HN	- HN S	HN O H

HN-R

HN-R

HN-R

HN-R

HN-R

HN-R

HN-R

HN-R

HN	HNOH	HN \	HN
HN	HN	HN	HN O N
HN	HN	HN	F HN N
HN	HN	HN F	HN
HN	HN	2 HN F	HN S
HN	HN	HNCOOH	HNO
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN	HN	HN	HN N CI
HN OH	HN		HN
HN	HN	HNOH	

HN-R

			·
HN	HN	HN	HN
HN	ÓН	LINI	Ö
HN	HN F	HN	HN
HN	HN	HN	F HN N
	HN	HN F .	HN
HN	HN	HN	HN
HN	F. 🐟	· F	HN
HN.	HN	HN COOH	HNO
HN	HNOH	HN NH ₂	HN
HN	HN O	HN HN Me	HN
HN	HN	HN	HN N CI
HNOH	HN		HN N
HN	HN	HN OH	

HN-R

HN-R

							-	
R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ^{1:}	³ R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	H	Cl	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ Oł	H Ph
Εt	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH	l ₂ H
iPr	Н	H	CH ₂ NHMe	Н	Н	Н	CH ₂ NHN	Ле Н
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Pł	н Н
nBu	Н	Н	COMe	Н	Н	Н	COMe	H
tBu	Н	Н	COOH	Н	Н	Н	COOF	l H
Ph	Н	H	CONH ₂	H	Н	Н	CONH	₂ H
Н	Et	Н	CONHMe	Εt	Н	Et	CONHI	ſe н
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHI	ls H
Н	nPr	Н	NHMs	nPr	Н	nP	r NHMs	Н
Н	nBu	H	NHCOMe	nBu	Н	nBı	NHCOM	ſe Н
Н	tBu	H '	NO_2	tBu	Н	tΒι	ı NO ₂	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Εt	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPi	r H	ОН
CI	Ph	Н	OH	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Εt	CI	CONHMe	Εt	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPı	r H	NHMs
H	Ph	- CI	NHMs	Ph	CI	Ph	Н	NO_2
Ме	Ме	Н	NO_2	Me	Н	Ме	Н.	OH
Et	Et	Н	ОН	Et	H	Et	. H	COMe
nPr	nPr	Н	COMe	nPr	Н	nΡι	r H	COOH
Ph	Ph	Н	COOH	Ph	Н	.Ph	Н	NO ₂

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R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	. H	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO ₃ F	i nPr
Н	Н	nBu	Cl	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	Н	tBu	H	Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ O	H Ph
Et	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH	¹ ₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHI	Ме Н
nPŗ	Н	Н	CH_2Ph	Н	Н	Н	CH ₂ PI	h H
nBu	Н	Н	COMe	Н	Н	Н	COMe	∍ Н
tBu	Н	H	COOH	Н	Н	Н	COOF	н н
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH	₂ H
Н	Et	Н	CONHMe	Et	H	Et	CONHI	Ле Н
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHI	/Is H
Н	nPr	Н	NHMs	nPr	H	nPr	NHMs	н
Н	nBu	H	NHCOMe	nBu	Н	nBu	NHCON	Ле Н
Н	tBu	H`	NO_2	tBu	Н	tBu	NO_2	H
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Εt	Н	SO₃H	Et	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	·OH
CI	Ph	Н	OH .	Ph	Н	Ph	H	COMe
Εt	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	H	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
Н	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	_. Me	Η	NO_2	Me	Н	Ме	Н.	ОH
Et	Et	Н	ОН	Εt	H	Et	Н	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	Н	. Ph	H .	NO_2
					·			

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R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	H	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ Oł	-l Ph
Εt	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NF	l ₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHN	Ие H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Pł	n H
nBu	Н	H	COMe	Н	Н	Н	COMe	H
tBu	Н	Н	COOH	Н	Н	Н	COOF	Н Н
Ph	Н	Н	CONH ₂	H	Н	Н	CONH	2 H.
Н	Et	Н	CONHMe	Et	H	Εt	CONHI	1e H
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHI	1s H
Н	nPr	Н	NHMs	nPr	H	nPr	NHMs	Н
Н	nBu	H _.	NHCOMe	nBu	Н	nBu	NHCOM	1e H
Н	tBu	Η '	NO_2	tBu	Н	tBu	NO_2	H
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Εt	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	OH	Ph	Н	Ph	Н	COMe
Εt	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
Н	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	Ме	Н	NO ₂	Ме	Н	Me	H.	ОН
Et	Et	Н	ОН	Et	H	Et	Н	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	H	COOH	Ph	H	. Ph	H	NO ₂

			_					
R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹	¹³ R ¹⁴	R ¹⁵
Н	Н	Et	NO_2	Н	Et	H	I NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHC) iPr
Η	Н	nPr	SO₃H	Н	nPr	Н	SO₃l	d nPr
Н	Н	nBu	CĪ	Н	nBu	Н		nBu
Н	Н	tBu	Br	Н	tBu	Н	l Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ O	H Ph
Et	Н	Н	CH_2NH_2	Н	H	Н	CH ₂ NI	H_2 H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NH	Ме н
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ P	h H
nBu	Н	Н	COMe	Н	Н	Н	COM	е Н
tBu	Н	Н	COOH	Н	Н	Н	COO	н н
Ph	Н	Н	CONH ₂	Н	Н	Н	CONF	Н ₂ Н
Н	Et	Н	CONHMe	Et	Н	E	t CONHI	Иe H
Н	iPr	H	CONHMs	iPr	Н	iP	r CONHI	Vis H
Н	nPr	Н	NHMs	nPr	Н	nΡ	r NHM	s H
Н	nBu	Н	NHCOMe	nBu	Н	nB	u NHCOI	Иe Н
Н	tBu	Н	NO_2	tBu	Н	tBı	u NO ₂	Н
Н	Ph	Η '	CHO	Ph	Н	Ph	ı H	SO₃H
CI	Et	H	SO₃H	Εt	Н	Et	: Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nΡ	r H	ОН
CI	Ph	Н	ОН	Ph	Н	Ph	n H	COMe
Et	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	Ci	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI ·	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Et	: Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nΡ	r H	NHMs
Н	Ph	CI	NHMs	Ph	CI	Ph	ı H	NO_2
Me	Me	Н	NO_2	Me	Н	Me	e H	OH
Et	Et	Н	ОН	Et	Н	Et	: H _,	COMe
nPr	'nPr	Н	COMe	nPr	H.	nΡ	r H	COOH
Ph	Ph	Н	СООН	Ph	Н	Ph	Н	NO ₂

										
R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵		R ¹³	R ¹⁴		R ¹⁵
H	H	Et	NO_2	Н	Et		Н	NO ₂	,	Et
Н	H	iPr	CHO	Н	iPr		Н	CHC		iPr
Н	Н	nPr	SO₃H	Н	nPr		Н	SO ₃ l	1	nPr
Н	H	nBu	CI	H	nBu		Н	CI		nBu
Н	Н	tBu	Br	Н	tBu		Н	Br		tBu
Н	Н	Ρh	CH ₂ OH	Н	Ph		Н	CH ₂ O	Н	Ph
Et	Н	Н	CH_2NH_2	Н	Н		Н	CH ₂ Ni	H_2	Н
iPr	Н	Н	CH ₂ NHMe	Н	Н		Н	CH ₂ NH	Ме	Н
nPr	Н	Н	CH ₂ Ph	Н	Н		Н	CH ₂ P	h	Н
nBu	Н	Н	COMe	Н	Н		Н	COM	9	Н
tBu	Н	Н	COOH	Н	Н		Н	COOF	-}	Н
Ph	Н	Н	CONH ₂	Н	Н		Н	CONH	2	Н
H	Et	Н	CONHMe	Et ·	Н		Et	CONH	/le	н
Н	iPr	H _.	CONHMs	iPr	Н		iPr	CONH	/ls	Н
Н	nPr	Н	NHMs	nPr	H		nPr	NHMs	;	Н
Н	nBu	Н	NHCOMe	nBu	Н	Į	nBu	NHCON	le	Н
Н	tBu	H	NO_2	tBu	Н	•	tBu	NO_2		Н
Н	Ph	Н	CHO .	Ph	Н		Ph	Н	;	SO₃H
CI	Εt	Н	SO₃H	Εt	Н		Et	Н		2NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	ı	nPr	Н		OH
CI	Ph	Н	ОН	Ph	Н		Ph	Н	C	COMe
Εt	CI	Н	COMe	Ci	Н		CI	CI	C	СООН
nPr	CI	Н	COOH	CI	Н		CI	CI	С	ONH ₂
Ph	CI	Н	CONH ₂	CI	Н		CI	CI		NHMe
H	Et	CI	CONHMe	Et	CI		Et	H		NHMs
H	nPr	CI	CONHMs	nPr	CI	r	ıPr	Н	Ν	IHMs
H	Ph	Cl	NHMs	Ph	Cl	I	⊃h	Н		NO_2
Me	Me	Н	NO_2	Ме	Н	N	Иe	H		OH
Et	Et	Н	ОН	Εt	H		Et	Ĥ	С	OMe
nPr	nPr	Н	COMe	nPr	Н	n	Pr	Н		ООН
Ph	Ph 	H	COOH.	Ph	H .	·	Ph	H ·		NO ₂
					•					

R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	· H	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO ₃ H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	l Ph
Εt	H	Н	CH ₂ NH ₂	H	Н	Н	CH ₂ NH	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHN	le H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	Н
nBu	Н	Н	COMe	Н	Н	H	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH ₂	2 H
Н	Et	Н	CONHMe	Εt	· H	Et	CONHM	le H
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	ls H
Н	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Н	nBu	Н	NHCOMe	nBu	Н	nBu	NHCOM	le H
Н	tBu	Η·	NO_2	tBu	Н	tBu	NO_2	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Et	Н	Et	Н	SO ₂ NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	ОН	Ph	Н	Ph	Н	COMe
Εt	CI	Н	COMe	CI	Н	Cl	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	Cl	CONHMe
Н	Et	CI	CONHMe	Et	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
H	Ph	CI	NHMs	Ph	CI	Ph	H	NO_2
Ме	Me	Н	NO_2	Me	Н	Ме	H	ОН
Et	Et	Н	ОН	Et	Н	Εt	H	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	H	Ph	H .	NO ₂

R ¹³	R ¹⁴	R ¹⁵	. R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
Н	Н	Et	NO ₂	Н	Et	Н	NO ₂	Et
Н	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	CI	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	Ph
Et	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH ₂	₂ H
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHM	le H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	H
nBu	Н	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	Ή
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH ₂	
Н	Et	H	CONHMe	Et	. Н	Εt	CONHM	
Н	iPr	Н	CONHMs	iPr	Н	iPr	CONHM	s H
Н	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Н	nBu	Н	NHCOMe	nBu	Н	nBu	NHCOM	e H
Н	tBu	Η·	NO_2	tBu	Н	tBu	NO_2	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO ₃ H	Et	Н	Et	Н	SO ₂ NHMe
CI	nPr	H	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	ОН	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	CI	Н	CI	CI	COOH
nPr	CI	Н	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Εt	CI	Et	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
H	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	Me	Н	NO_2	Me	Н	Ме	Н	ОН
Et	· Et	H	ОН	Εt	Н	Et	H	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	H	Ph	H ·	NO ₂

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R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵	R ¹³	R ¹⁴	R ¹⁵
	Н	Et	NO_2	Н	Et	Н	NO ₂	Et
H	Н	iPr	CHO	Н	iPr	Н	CHO	iPr
Н	Н	nPr	SO₃H	Н	nPr	Н	SO₃H	nPr
Н	Н	nBu	CI	Н	nBu	Н	Cl	nBu
Н	Н	tBu	Br	Н	tBu	Н	Br	tBu
Н	Н	Ph	CH ₂ OH	Н	Ph	Н	CH ₂ OH	Ph
Et	Н	Н	CH ₂ NH ₂	Н	Н	Н	CH ₂ NH ₂	- •
iPr	Н	Н	CH ₂ NHMe	Н	Н	Н	CH ₂ NHM	le H
nPr	Н	Н	CH ₂ Ph	Н	Н	Н	CH ₂ Ph	Н
nBu	Н	Н	COMe	Н	Н	Н	COMe	Н
tBu	Н	Н	COOH	Н	Н	Н	COOH	Н
Ph	Н	Н	CONH ₂	Н	Н	Н	CONH ₂	*
Н	Et	H	CONHMe	Εt	· H	Εt	CONHM	
Н	iPr	Н	CONHMs	iPr	H	iPr	CONHM	s H
Н	nPr	Н	NHMs	nPr	Н	nPr	NHMs	Н
Н	nBu	Н	NHCOMe	nBu	Н	nBu	NHCOM	e H
Н	tBu	ΗЧ	NO_2	tBu	Н	tBu	NO_2	Н
Н	Ph	Н	CHO	Ph	Н	Ph	Н	SO₃H
CI	Et	Н	SO₃H	Εt	Н	Εt	Н	SO_2NHMe
CI	nPr	Н	SO ₂ NHMe	nPr	Н	nPr	Н	ОН
CI	Ph	Н	ОН	Ph	Н	Ph	Н	COMe
Et	CI	Н	COMe	Cl	Н	CI	CI	COOH
nPr	CI	H	COOH	CI	Н	CI	CI	CONH ₂
Ph	CI	Н	CONH ₂	CI	Н	CI	CI	CONHMe
Н	Et	CI	CONHMe	Et	CI	Εt	Н	CONHMs
Н	nPr	CI	CONHMs	nPr	CI	nPr	Н	NHMs
Ħ	Ph	CI	NHMs	Ph	CI	Ph	Н	NO_2
Me	Ме	Н	NO_2	Me	Н	Me	H	OH
Et	· Et	Н	ОН	Et	H	Εt	H	COMe
nPr	nPr	Н	COMe	nPr	Н	nPr	Н	COOH
Ph	Ph	Н	COOH	Ph	H	Ph 	H .	NO ₂

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	H	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	H	Н	Н	CHO
Н	Н	nPr	Н	SO ₃ H	Н	Н	ÆН	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	Cl
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Н	Ме	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Εt	Ph	Ме	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	H	Ме	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	H	COMe
Me	tBu	Н	Me	COOH	Н	Ме	Н	COOH
Εt	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	H	Εt	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	_. nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph 、	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	OH	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH_2NH_2	Et	Н
CH_2NH_2	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Me	CH ₂ NHMe	Me	Н
CH₂Ph	Εt	Et	CH ₂ Ph	OH	Εt	CH ₂ Ph	Et	Н
CH₂Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph ·	CH ₂ CH ₂ Ph	Ph	H

							•	
R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
H	H	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	H	Н	SO ₃ H
Н	Н	nBu	Н	Cl	Н	Н	Н	· CI
Н	Н	tBu	Н	Br	Н	H	Н	Br
Me	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Ме	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Ме	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Ме	Н	CH ₂ Ph
Ме	nBu	Н	Me	COMe	Н	Mè	Н	COMe
Me	tBu	Н	Me	COOH	Н	Ме	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Εt	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph 、	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO ₃ H	Et	Ph	Εt	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	Cl
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et.	CH ₂ NH ₂	CONHMe	Et	CH_2NH_2	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH₂Ph	Εt	Et	CH₂Ph	ОН	Et	CH ₂ Ph	Et	H
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH₂Ph	nPr	Н
CH ₂ CH ₂ Ph	Ρh	Ph	CH ₂ CH ₂ Ph	COOH	Ph ·	CH ₂ CH ₂ Ph	Ph 	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	СНО	Н	Н	H	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
н	Н	nBu	Н	Cl	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Ме	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Ме	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Εt	CONHMe
Εt	H	iPr	Εt	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH₂OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH₂OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH ₂ Ph	Εt	Et	CH ₂ Ph	ОН	Εt	CH₂Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH₂Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	<u>——</u> Н	Н	Н	NO ₂
H	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Ή	Br
Me	H	Н	Me	CH ₂ OH	Н	Ме	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Εt	CONHMe
Et	Н	iPr	Εt	CONHMs	iPr	Et	iPr	CONHMs
iPr	H	nPr	iPr	NHMs	nPr	iPr ·	nPr	NHMs
nPr	H	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO ₂	tBu	nBu	tBu	NO_2
⊨tBu	Н	Ph t	tBu	CHO	Ph	tBu	Ph	H
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH_2NH_2	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH_2NH_2	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH₂Ph	Εt	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH₂Ph	COMe	nPr	CH₂Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph ·	CH ₂ CH ₂ Ph	Ph	Н
			——————————————————————————————————————					

Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COOH Me tBu H Me COOH H Me H COOH Me tBu H Me COOH H Me H COOH Et Ph H Et COOH H Me H COOH Et Ph H Et COOH H Et H COOH COOH Me Me COOH Me Me Me COOH Me Me NPC NPC NPC NPC NPC NPC NPC NPC NPC Me NPC NPC Me NPC NPC NPC NPC NPC NPC NPC NPC <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th>*</th> <th></th>								*	
H H H IPT H CHO H H H CHO H H H NPT H SO ₃ H H H H SO ₃ H H H NBU H CI H H H CI H H H BBU H BF H H H BF Me H CH ₂ OH ME CH ₂ NH ₂ H Me H CH ₂ NH Me IPT H Me CH ₂ NH H Me H CH ₂ NH Me nPT H Me CH ₂ NH H Me H CH ₂ NH Me nBU H Me COME H ME H COME Me tBU H ME COMH H ME H COME Me tBU H ME COOH H ME H COME Et Ph H Et CONH ₂ H Et H CONH Et H IPT Et CONHMS IPT Et IPT CONHMS IPT H NPT IPT NHMS NPT IPT NHMS NPT H NBU NPT NHCOME NBU NPT NHCOME NBU H TBU NO ₂ TBU NBU NO ₂ TBU H TBU NO ₂ TBU H NBU NO ₂ TBU NHCOME TBU H TBU NO ₂ TBU NHCOME TCH2PH TBU CH2PH TBU TCH2PH TCH2NH2 CI CH2PH TCH2PH TBU CH2PH TCH2PH TCH2PH TBU CH2PH TCH2PH TCH2PH TBU CH2PH TCH2PH TCH2PH TCH2PH TCH2PH TCH2PH TC	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
H H NPT H SO3H H H H CI H H NBU H CI H H H CI H H H BT H BT H H H BT Me H H H Me CH2OH H Me H CH2NH Me Et Ph Me CH2NH2 H Me H CH2NH Me iPr H Me CH2NH H Me H CH2NH Me nPr H Me COME H Me H CH2PH Me nBU H Me COME H Me H COME Et Ph H Me COME H ME H COME Et Ph H Et CONH2 H Et H CONH Et H H ET CONHM IPT BT NHMS ET H NPT IPT NHMS NPT IPT NHMS NPT H NBU NPT NHCOME NBU NPT NBU NHCOME NBU H NO2 UBU NBU UBU NO2 ET Ph ET CONHME IT PH NHMS NPT NHCOME NBU H NPT NHCOME NBU NPT NBU NHCOME NBU H NPT NHCOME NBU NPT NBU NHCOME NBU H BU ND2 UBU ND2 UBU ND4 ET Ph ET CONHME ET ET Ph ET H H CH2OH CI PH CH2OH SO3H ET Ph ET H CH2OH CI PH CH2OH COME CI CH2OME CI CI CH2OME ET CI CH2OME COME CI CH2OME CI CI CH2OME TO CH2NH2 CONHMS NPT CH2OME CI CI CH2NH2 PH CH2OH COH CI CH2NH2 ET H CH2NH2 PH CI CH2NH2 CONHME ET CH2NH2 ET H CH2NH2 H ET CH2NH2 CONHME CI CH2NH2 ET H CH2NH2 H ET CH2NH2 CONH CI CH2NH2 CI CI CH3NH2 H ET CH2NH2 CONH CI CH2NH2 ET H CH2NH2 H PP CH2NH2 CONHME ET CH2NH2 ET H CH2NH2 H PP CH2NH2 CONHME ET CH2NH2 ET H CH2NH2 H PP CH2NH2 NHMS PP CH2NH2 PP H CH2NH4 ME CH2NH4 NO2 ME CH2NH4 ME H CH2NH4 ME CH2NH4 NA CH3NH4 NA	Н	Н	Et	Н	NO ₂	Н	Н	Н	
H H H BBU H CI H H H CI H H H BBU H BF H H H BF Me H H H Me CH₂OH H Me H CH₂OH Me Et Ph Me CH₂NH₂ H Me H CH₂NHM Me iPr H Me CH₂NHMe H Me H CH₂NHM Me nPr H Me CH₂NHMe H Me H CH₂Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COMH H Me H COMH Et Ph H Et CONH₂ H Et Et CONHM₂ Et H BI FF ET CONHME ET ET ET CONHM⅓ iPr H nPr iPr NHMS nPr iPr nPr NHMS iPr H nBu nPr NHCOME nBu nPr nBu NHCOM€ nBu H tBu nBu NO₂ tBu nBu tBu NO₂ tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO₃H Et Ph Et H CH₂OH CI nPr CH₂OH SO₂NHME nPr CH₂OH Ph H CH₂OME ET CI CH₂OME COME CI CH₂OME CI CI CH₂OME TE CI CH₂OME COME CI CH₂OME CI CI CH₂OME Ph CH₂OH CONHMS NPR CH₂OME CI CI CH₂OME NPR CH₂OH CONHMS NPR CH₂OME CI CI CH₂OME Ph CH₂OME COME CI CH₂OME CI CI CH₂OME Ph CI CH₂OME COME CI CH₂OME CI CI CH₂OME Ph CH₂OME COME CI CH₂OME CI CI CH₂OME Ph CH₂OME COMH CI CH₂OME CI CI CH₂OME Ph CH₂OME COME CI CH₂OME CI CI CH₂NH₂ Ph CI CH₂OME CONHMS NPR CH₂NH₂ ET H CH₂NH₂ Ph CI CH₂NH₂ CONHMS NPR CH₂NH₂ Ph H CH₂NH₂ H PP CH₂NH₂ NHMS Ph CH₂NH₂ Ph H CH₂NHME ME ME CH₂NHME NO₂ ME CH₂NHME ME H CH₂Ph ET CH₂PH OH ET CH₂PH ET H CH₂PH DPR CH₂PH OH ET CH₂PH ET H CH₂PH DPR CH₂PH COME NPR CH₂PH RPR H CH₂PH NPR CH₂PH RPR CH₂PH RPR H CH₂PH NPR CH₂PH COME NPR CH₂PH RPR H CH₂PH RPR CH₂PH COME NPR CH₂PH RPR H CH₂PH RPR CH₂PH COME NPR CH₂PH RPR H CH₂PH RPR CH₂PH RPR CH₂PH RPR CH₂PH RPR CH₂PH CH₂PH RPR CH₂PH RPR CH₂PH CH₂PH RPR CH₂PH CH₂P	H	H	iPr	Н	CHO	Н	Н	Н	CHO
H H H tBu H Br H H H Br Me H H H Me CH₂OH H Me H CH₂OH Me Et Ph Me CH₂NH₂ H Me H CH₂NH₂ Me iPr H Me CH₂NHMe H Me H CH₂NHM Me nPr H Me CH₂Ph H Me H CH₂Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COOH Et Ph H Et CONH₂ H Et H COOH Et H Et Et CONHMe Et Et Et CONHMS iPr H nPr iPr NHMs nPr iPr nPr NHMs nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu NO₂ tBu nBu tBu NO₂ tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO₃H Et Ph Et H CH₂OH CI nPr CH₂OH SO₂NHMe nPr CH₂OH nPr H CH₂OH CI Ph CH₂OH COME CI CH₂OME CI CI CH₂OME nPr CI CH₂OME COOH CI CH₂OME CI CI CH₂OME nPr CI CH₂OME COOH CI CH₂OME CI CI CH₂OH2 H Et CH₂NH₂ CONHµ₂ Et H CH₂NH2 H Ph CH₂NH₂ CONHµ₂ CI CH₂NH₂ CH₂NH2 H ET CH₂NH2 CONHµ2 CI CH₂NH2 ET H CH₂NH2 H Ph CH₂NH2 CONHµ2 CI CH₂NH2 ET H CH₂NH2 H Ph CH₂NH2 CONHµ2 CI CH₂NH2 ET H CH₂NH2 H Ph CH₂NH2 CONHµ3 nPr CH₂NH2 Ph H CH₂NH2 H Ph CH₂NH2 CONHMB NPR CH₂NH2 Ph H CH₂NH2 H Ph CH₂NH2 CONHMB NPR CH₂NH2 Ph H CH₂NH4 H Ph CH₂NH2 CONHB ET CH₂NH2 Ph H CH₂NH4 ME CH₂NH4 NO₂ ME CH₂NH4 Ph H CH₂NH4 ME CH₂NH4 NO₂ ME CH₂NH4 Ph H CH₂NHME ME ME CH₂NHME NO₂ ME CH₂NHME ME H CH₂Ph ET CH₂NHME NO₂ ME CH₂NHME ME H CH₂Ph ET CH₂NHME NO₂ ME CH₂NHME ME H CH₂Ph ET CH₂NHME NO₂ ME CH₂NHME ME H	Н	Н	nPr	Н	SO₃H	Н	Н	Н	
Me H H Me CH₂OH H Me H CH₂OH Me Et Ph Me CH₂NH₂ H Me H CH₂NHM Me iPr H Me CH₂NHMe H Me H CH₂NHMMe Me nPr H Me CH₂Ph H Me H CH₂Ph Me nBu H Me COMe H Me H CM₂Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Et Ph H Et CONHMe Et Et Et CONHMe Et H Ph F NHMs nPr IPr NHMs NPr NPr	Н	H	nBu	Н	CI	Н		Н	
Me Et Ph Me CH ₂ NH ₂ H Me H CH ₂ NH ₂ Me iPr H Me CH ₂ NHMe H Me H CH ₂ NHM Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMH H Me H COMe Me tBu H Me COOH H Me H COME Et Ph H Et CONH H Me H COOH H L COOH H COOH COOH L Et Et CT COOH COOH De De De De De De De De	ъH	Н	tBu	Н	Br	Н		Н	
Me iPr H Me CH ₂ NHMe H Me H CH ₂ NHM Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COMe Et Ph H Et CONH H Et H CONH Et Ph H Pt Et CONHMS iPr Et Et CONHMS iPr H nPr iPr NHMS nPr iPr NHMS nPr iPr NHMS NPr NHMS NPr nPr NHMS NPr NHMS	Me	Н	Н	Me	CH ₂ OH	Н	Ме	Н	
Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COOH Me tBu H Me COOH H Me H COOH Me tBu H Me COOH H Me H COOH Et Ph H Et COOH H Me H COOH Et Ph H Et COOH H Et H COOH COOH Me Me COOH Me Me Me COOH Me Me NPC NPC NPC NPC NPC NPC NPC NPC NPC Me NPC NPC Me NPC NPC NPC NPC NPC NPC NPC NPC <td>Me</td> <td>Et</td> <td>Ph</td> <td>Me</td> <td>CH₂NH₂</td> <td>Н</td> <td></td> <td></td> <td></td>	Me	Et	Ph	Me	CH ₂ NH ₂	Н			
Me nBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe COMe L L COMe L L COMe COMe N N N COMe N	Me	iPr	Н	Me	CH ₂ NHMe	Н		Н	CH ₂ NHMe
Me tBu H Me COOH H Me H COOH Et Ph H Et CONH ₂ H Et H CONH ₂ Et H Et Et CONHME Et Et Et CONHME Et H iPr Et CONHMS iPr Et iPr CONHMS iPr H nPr iPr NHMS nPr iPr nPr NHMS nPr H nBu nPr NHCOME nBu nPr nBu NHCOME nBu H tBu nBu NO ₂ tBu nBu tBu NO ₂ tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO ₃ H Et Ph Et H CH ₂ OH CI nPr CH ₂ OH SO ₂ NHME nPr CH ₂ OH nPr H CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OME Et CI CH ₂ OME COME CI CH ₂ OME CI CI CH ₂ OME nPr CI CH ₂ OME COOH CI CH ₂ OME CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H Ph CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ Ph H CH ₂ NH ₂ H Ph CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ Ph H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMS Ph CH ₂ NH ₂ Ph H CH ₂ NHME ME ME CH ₂ NHME NO ₂ ME CH ₂ NHME ME H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H CH ₂ Ph RPr NPr NPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr NPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr NPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr NPr CH ₂ Ph COME nPr CH ₂ Ph nPr H	Me	nPr	Н	Me	CH₂Ph	Н		Н	-
Et Ph H Et CONH ₂ H Et H CONH ₂ Et H Et Et CONHMe Et Et Et CONHMe Et H iPr Et CONHMS iPr Et iPr CONHMS iPr H nPr iPr NHMS nPr iPr nPr NHMS nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu NO ₂ tBu nBu tBu NO ₂ tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO ₃ H Et Ph Et H CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr H CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI CI CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H Ph CH ₂ NH ₂ CONHME TO CH ₂ NH ₂ Ph H CH ₂ NH ₂ H Ph CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ Ph H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMS Ph CH ₂ NH ₂ Ph H CH ₂ NHME ME ME CH ₂ NHME NO ₂ ME CH ₂ NHME ME H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H CH ₂ Ph nPr nPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr nPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr nPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr nPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr nPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr nPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CH ₂ Ph nPr nPr CH ₂ Ph COME nPr CH ₂ Ph nPr H CONHME NP	Me	nBu	Н	Me	COMe	H			
Et H Et Et CONHMe Et Et Et CONHMe Et H iPr Et CONHMs iPr Et iPr CONHMs iPr H nPr iPr NHMs nPr iPr nPr NHMs nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu NO2 tBu nBu tBu NO2 tBu H Ph tBu CHO Ph tBu Ph H Ph Cl Et Ph SO3H Et Ph Et H CH2OH Cl nPr CH2OH SO2NHMe nPr CH2OH nPr H CH2OH Cl Ph CH2OH OH Ph CH2OH Ph H CH2OME Et Cl CH2OME COME Cl CH2OME Cl Cl CH2OME TO CH2OME COOH Cl CH2OME Cl Cl CH2NH2 Ph Cl CH2NH2 CONHME Et CH2NH2 Cl Cl CH2NH2 H Et CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H nPr CH2NH2 CONHMS nPr CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NHME ME ME CH2NHME NO2 ME CH2NHME ME H CH2Ph Et Et CH2Ph OH Et CH2Ph Et H CH2Ph nPr nPr CH2Ph COME nPr CH2Ph nPr H	Me	tBu	Н	Me	COOH	Н		Н	
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nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu nBu NO2 tBu nBu tBu NO2 tBu nBu tBu NO2 tBu nBu tBu NO2 tBu nBu tBu NO4 tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO3H Et Ph Et H CH2OH CI nPr CH2OH SO2NHMe nPr CH2OH nPr H CH2OH CI Ph CH2OH OH Ph CH2OH Ph H CH2OME CI CI CH2OME CI CI CH2OME CI CI CH2OME CI CI CH2OME NPr CI CH2OME COOH CI CH2OME CI CI CH2NH2 Ph CI CH2NH2 CONH2 CI CI CH2NH2 Ph CI CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H Ph CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H Ph CH2NH2 CONHMS nPr CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NHME ME CH2NHME NO2 ME CH2NHME ME H CH2Ph nPr CH2Ph COME NPr CH2Ph nPr H CH2Ph nPr CH2Ph COME NPR CH2Ph NPR CH2	Et	Н	iPr	Et	CONHMs	iPr		iPr	
nBu H tBu nBu NO2 tBu nBu tBu NO2 tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO3H Et Ph Et H CH2OH CI nPr CH2OH SO2NHMe nPr CH2OH nPr H CH2OH CI Ph CH2OH OH Ph CH2OH Ph H CH2OME Et CI CH2OME COME CI CH2OME CI CI CH2OME nPr CI CH2OME COOH CI CH2OME CI CI CH2NH2 Ph CI CH2NH2 CONH2 CI CH2NH2 CI CI CH2NH2 H Et CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H nPr CH2NH2 CONHME Et CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NHME ME ME CH2NHME NO2 ME CH2PH ME H CH2Ph Et Et CH2Ph OH Et CH2Ph nPr H	iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	
tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO ₃ H Et Ph Et H CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr H CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI CI CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMS Ph CH ₂ NH ₂ Ph H CH ₂ NHME ME ME CH ₂ NHME NO ₂ ME CH ₂ NHME ME H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H	nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
Ph CI Et Ph SO ₃ H Et Ph Et H CH ₂ OH on Pr CH ₂ OMe on Pr CH ₂ OMe on Pr CI ch ₂ OMe on Pr CI ch ₂ OMe on COMe on CI ch ₂ OMe on CI	nBu	٠H	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr H CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI CI CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph CH ₂ NH ₂ Ph H CH ₂ NHMe Me Me CH ₂ NHMe NO ₂ Me CH ₂ NHMe Me H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H CH ₂ Ph nPr COMe nPr CH ₂ Ph nPr H	tBu	Н	Ph 、	tBu	CHO	Ph	tBu	Ph	Н
CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMS Ph CH ₂ NH ₂ Ph H CH ₂ NHME ME ME CH ₂ NHME NO ₂ ME CH ₂ NHME ME H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H	Ph	CI	Et	Ph	SO₃H	Et	Ph	Et	
CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI CI CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMS Ph CH ₂ NH ₂ Ph H CH ₂ NHME ME ME CH ₂ NHME NO ₂ ME CH ₂ NHME ME H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H	CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	
CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMS Ph CH ₂ NH ₂ Ph H CH ₂ NHME ME ME CH ₂ NHME NO ₂ ME CH ₂ NHME ME H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H		CI	Ph	CH ₂ OH	ОН	Ph	_		
CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph CH ₂ NH ₂ Ph H CH ₂ NHMe Me Me CH ₂ NHMe NO ₂ Me CH ₂ NHMe Me H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph Et H CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr H	CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI		CI	
CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph CH ₂ NH ₂ Ph H CH ₂ NHMe Me Me CH ₂ NHMe NO ₂ Me CH ₂ NHMe Me H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph Et H CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr H	CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH_2NH_2	Et	Н
CH_2NH_2 H Ph CH_2NH_2 NHMs Ph CH_2NH_2 Ph H CH_2NHMe Me CH_2NHMe Me CH_2NHMe Me CH_2NHMe Me CH_2Ph Et Et CH_2Ph OH Et CH_2Ph Et H CH_2Ph nPr CH_2Ph COMe nPr CH_2Ph nPr H	CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	
CH $_2$ NHMe Me Me CH $_2$ NHMe NO $_2$ Me CH $_2$ NHMe Me H CH $_2$ Ph Et Et CH $_2$ Ph OH Et CH $_2$ Ph Et H CH $_2$ Ph nPr nPr CH $_2$ Ph COMe nPr CH $_2$ Ph nPr H		Н	Ph	CH ₂ NH ₂	NHMs	Ph		Ph	
CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph Et H CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr H		Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	
CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr H		Εt	Et	CH ₂ Ph	ОН	Et		Et	
		nPr	nPr	_	COMe	nPr	CH ₂ Ph		
	_	·Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph·	CH ₂ CH ₂ Ph	Ρ́h	H

Me Et Ph Me CH ₂ NH ₂ H Me H CH ₂ NH ₂ Me iPr H Me CH ₂ NHMe H Me H CH ₂ NHM Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COOH Et Ph H Et CONH ₂ H Et H CONH ₂ Et H Et Et CONHMe Et Et Et CONHM Et H iPr Et CONHMS iPr Et iPr CONHM iPr H nPr iPr NHMS nPr iPr nPr NHMS										
H H H iPr H CHO H H H CHO H H H nPr H SO₃H H H H SO₃H H H H nBu H CI H H H H CI H H H Bu H Br H H H Br Me H H Me CH₂OH H Me H CH₂NH Me iPr H Me CH₂NHMe H Me H CH₂NH Me nPr H Me CH₂NHMe H Me H CH₂NH Me nBu H Me CH₂Ph H Me H CH₂NH Me nBu H Me COME H Me H CH₂NH Me tBu H Me COMH H Me H COMH Et Ph H Et CONH₂ H Et H CONH Et H iPr Et CONHMS iPr Et iPr CONHM iPr H nBu nPr NHCOME nBu nPr nBu NHCOM nBu H tBu NO₂ tBu nBu tBu NO₂ tBu H DP SO₃H Et Ph H H H H H COMH CH₂OH CI nPr CH₂OH OH Ph CH₂OH Ph H CH₂OH CI nPr CH₂OH OH Ph CH₂OH Ph H CH₂OH CI nPr CH₂OH COMH Et Et H CH₂OH CI nPr CH₂OH COMH CI CH₂OM CI CI CH₂OME nPr CI CH₂OH COMH CI CH₂OME CI CI CH₂OME nPr CI CH₂OME COMH CI CH₂OME CI CI CH₂OME NPR CH₂OH COMH CI CH₂OME CI CI CH₂OH CI CH₂OME COMH CI CH₂OME CI CI CH₂OH CI CH₂OME COMH CI CH₂OME CI CI CH₂OME NPR CI CH₂OME COMH CI CH₂OME CI CI CH₂OME NPR CI CH₂OME COMH CI CH₂OME CI CI CH₂OME TRICLE THE CH₂OME COMH CI CH₂OME CI CI CH₂OME NPR CI CH₂OME COMH CI CH₂OME CI CI CH₂OME NPR CI CH₂OME COMH CI CH₂OME CI CI CH₂OME NPR CI CH₂OME COMH CI CH₂OME CI CI CH₂OME NPR CH₂OME NPR CH₂OME ME H CH₂OH CH₂OH OH Ph CH₂OME ME H CH₂OH CH₂OH OH Ph		R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
H H H nPr H SO₃H H H H SO₃H H H H nBu H Cl H H H H Cl H H H tBu H Br H H H Br Me H H Me CH₂OH H Me H CH₂OH Me Et Ph Me CH₂NHMe H Me H CH₂NHM Me iPr H Me CH₂NHMe H Me H CH₂NHM Me nPr H Me CH₂NHMe H Me H CH₂NHM Me nBu H Me COMe H Me H COµ Et Ph H Me COOH H Me H COOH Et Ph H Et CONH₂ H Et H CONH₂ Et H Et Et CONHME Et Et Et Et CONHM Et H IPr Et CONHME Et Et Et Et CONHM Et H IPr Et CONHMS iPr Et iPr CONHM iPr H nPr iPr NHMS nPr iPr nPr NHMS nPr H nBu nPr NHCOMe nBu nPr nBu NHCOM nBu H tBu NO₂ tBu nBu tBu NO₂ tBu H Ph tBu CHO Ph tBu Ph Et H CH₂OH Cl Ph CH₂OH OH Ph CH₂OH Ph H CH₂OME Et Cl CH₂OME COOH Cl CH₂OH Cl Cl CH₂OME TR CH₂OH COOH Cl CH₂OH Cl Cl CH₂OME TR CH₂OH COOH Cl CH₂OH Cl Cl CH₂OME NPr CH₂OH COOH Cl CH₂OH Cl Cl CH₂NH₂ Ph Cl CH₂NH₂ CONHME Et CH₂NH₂ Et H CH₂OH H Ph CH₂OH COOH Cl CH₂OH Cl Cl CH₂NH₂ Ph Cl CH₂NH₂ CONHME Et CH₂NH₂ Et H CH₂OH L CH CH₂NH₂ CONHME ET CH₂NH₂ ET H CH₂OH Cl Ph CH₂OH COOH Cl CH₂OHE Cl Cl CH₂NH₂ Ph Cl CH₂NH₂ CONHME ET CH₂NH₂ ET H CH₂NH₂ H Ph CH₂NH₂ CONHME ET CH₂NH₂ ET H CH₂NH₂ H Ph CH₂NH₂ CONHME ET CH₂NH₂ ET H CH₂NH₂ H Ph CH₂NH₂ CONHME ET CH₂NH₂ ET H CH₂NH₂ H Ph CH₂NH₂ NHMS Ph CH₂NH½ Ph H CH₂NH2 H Ph CH₂NH2 NHMS Ph CH₂NHME ME H CH₂Ph ET CH₂Ph OH ET CH₂Ph ET H		Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
H H H CI H H H CI H H H Br H H H Br Me H H Me CH₂OH H Me H CH₂OH Me H H Me CH₂OH H Me H CH₂OH Me IPr H Me CH₂OH H Me H CH₂OH Me IPr H Me CH₂OH H Me H CH₂OH Me nBu H Me COMe H Me H COMe Me nBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Et Ph H Et COMe COMe H Me H COMe Bu H Bu </td <td></td> <td>Н</td> <td>Н</td> <td>iPr</td> <td>Н</td> <td>CHO</td> <td>Н</td> <td>Н</td> <td>Н</td> <td></td>		Н	Н	iPr	Н	CHO	Н	Н	Н	
H H H H H H H H H CH₂OH Me H H Me CH₂OH H Me H CH₂OH Me Et Ph Me CH₂NH₂ H Me H CH₂OH Me iPr H Me CH₂NHMe H Me H CH₂NHM Me nPr H Me CH₂Ph H Me H CH₂Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Et Ph H Et CONHMe Et Et Et CONHMe Et H iPr Et CONHMe iPr Et Et CONHMe		Н	Н	nPr	Н	SO₃H	Н		Н	
Me H H Me CH2OH H Me H CH2OH Me Et Ph Me CH2NH2 H Me H CH2NHM Me iPr H Me CH2NHMe H Me H CH2NHM Me nPr H Me CH2Ph H Me H CH2Ph Me nBu H Me COMe H Me H COMe Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COMe Et Ph H Et CONHM Et Et H CONHM Et H H Et CONHM ipr Et Et CONHM ipr H nPr Et CONHM ipr ipr NHMs nPr ipr		Н	Н	nBu	Н	CI	Н		H	
Me Et Ph Me CH ₂ NH ₂ H Me H CH ₂ NH, CH ₂ NH Me iPr H Me CH ₂ NH, CH ₂ NH H Me H CH ₂ NH, CH ₂ NH Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COMe Me tBu H Me COOH H Me H COOH Et Ph H Et CONH H Et Et CONH Et H Ph Et CONHM Et Et Et CONHM ipr H nPr NHCOM nBu nPr NHMs NPr		Н	Н	tBu	Н	Br	Н		H	
Me iPr H Me CH ₂ NHMe H Me H CH ₂ NHMe Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COMe Et Ph H Et CONHMe Et Et H CONHMe Et H iPr Et CONHMe Et Et Et CONHME iPr H nPr iPr NHMs nPr iPr CONHM iPr H nPr iPr NHMs nPr iPr NHMs nPr H nPr NHMs nPr iPr nPr NHMs nPr H		Me	Н	Н	Me	CH ₂ OH	Н		Н	CH ₂ OH
Me nPr H Me CH ₂ Ph H Me H CH ₂ Ph Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COMe Et Ph H Et COOH H Me H COOH Et Ph H Et CONHME Et Et H CONHME Et H ipr Et CONHME Et Et Et CONHME ipr H npr ipr Det ipr CONHME Et Et Et CONHME Et Et Et CONHME Et Et Ipr CONHME Ipr Ipr CONHME Ipr Ipr Ipr CONHME Ipr		Me	Εt	Ph	Me	CH ₂ NH ₂	Н		Н	CH_2NH_2
Me nBu H Me COMe H Me H COMe Me tBu H Me COOH H Me H COOH Et Ph H Et COOH H Me H COOH Et Ph H Et COOH H Me H COOH Et Ph H Et COOH H Me H COOH Et Ph H Et COOH H Et Et COOH COH IP H nPr Et COOH NPr H NPr NPr <td></td> <td>Me</td> <td>iPr</td> <td>Н</td> <td>Me</td> <td>CH₂NHMe</td> <td>Н</td> <td>Ме</td> <td>Н</td> <td>CH₂NHMe</td>		Me	iPr	Н	Me	CH ₂ NHMe	Н	Ме	Н	CH ₂ NHMe
Me tBu H Me COOH H Me H COOH Et Ph H Et CONH2 H Et H COOH Et Ph H Et CONHMB Et Et Et CONHMB Et H IPr Et CONHMB IPr Et Et CONHMB IPr H nPr Et CONHMB IPr Et Et CONHMB IPr H nPr IPr NHMS nPr IPr NHMS nPr H nBu nPr NHCOMB nBu nPr NHMS nPr H nBu nPr NHCOMB nBu nPr NHMS nPr H nBu nPr NHMS nPr IPr NHMS NPr IPr NHMS NPr NHMS NPr NPr NHMS NPr NPr NPr NPr NPr		Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	
Et Ph H Et CONH ₂ H Et H CONH ₂ Et H Et Et Et Et Et Et CONHM Et H iPr Et CONHMS iPr Et iPr CONHM iPr H iPr Et CONHMS iPr Et iPr CONHMS iPr H nPr iPr NHMS nPr iPr NHMS nPr H nBu nPr NHCOM nBu nPr NHMS nPr H nBu nPr NHCOM nBu nPr NHMS nBu H nBu nPr NHCOM nBu nPr nBu NHCOM nBu H tBu nPr NHCOM nBu nPr nBu NHCOM nBu H tBu nPr NHCOM nBu nPr NHCOM nBu nBu nBu		· Me	nBu	Н	Me	COMe	Н	Ме	Н	
Et H Et Et CONHMe Et Et Et CONHM Et H iPr Et CONHMS iPr Et iPr CONHM iPr H nPr iPr NHMs nPr iPr nPr NHMs nPr H nPr iPr NHMs nPr iPr nPr NHMs nPr H nPr iPr NHCOM nBu nPr nPr NHMs nPr H nBu nPr NHCOM nBu nPr nBu NHCOM nBu H tBu nPr NHCOM nBu nPr nBu NHCOM nBu H tBu nPu NHCOM nBu nPr nBu NHCOM nPr NHCOM NPr CH2OH DPr NHCOM		Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et H iPr Et CONHMs iPr Et iPr CONHM iPr H nPr iPr NHMs nPr iPr nPr NHMs nPr H nBu nPr NHCOMe nBu nPr nBu NHCOM nBu H tBu nBu NO2 tBu nBu tBu NHCOM nBu H tBu nBu NO2 tBu nBu tBu NHCOM nBu H tBu nBu NO2 tBu nBu tBu NHCOM nBu H tBu nBu NO2 tBu nBu tBu NHCOM tBu H tBu nBu NO2 tBu nBu tBu NO2 tBu H tBu CHO Ph tBu tBu NO2 TBu tBu NO2 TBu tBu NHCOM TBu TBu TBu TB		Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
iPr H nPr iPr NHMs nPr iPr nPr NHMs nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu nBu nBu nBu nBu NHCOMe tBu H tBu nBu nBu tBu nBu tBu nBu tBu nBu NHCOMe nBu NHCOMe NHCOMe nBu nBu NHCOMe NHCOMe nBu NHCOMe N		Et	Н	Et	Et	CONHMe	Et	Et	Εt	CONHMe
nPr H nBu nPr NHCOMe nBu nPr nBu NHCOMe nBu H tBu nBu NO2 tBu nBu tBu NO2 tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO3H Et Ph Et H CH2OH CI Ph CH2OH SO2NHMe nPr CH2OH nPr H CH2OH CI Ph CH2OH OH Ph CH2OH nPr H CH2OH CI CH2OH OH Ph CH2OH Ph H H H H H H H CH2OH COH CH2OH		Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
nBu H tBu nBu NO2 tBu nBu tBu NO2 tBu hBu tBu NO2 tBu H Ph tBu CHO Ph tBu Ph H H Ph CI Et Ph SO3H Et Ph Et H CH2OH CI nPr CH2OH SO2NHMe nPr CH2OH nPr H CH2OH CI CH2OH CI CH2OH OH Ph CH2OH Ph H CH2OH Ph H CH2OH CI CI CH2OME CI CI CH2NH2 Ph CI CH2NH2 CONH2 CI CI CH2NH2 CI CI CH2NH2 TH Et CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H Ph CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H Ph CH2NH2 CONHMS nPr CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NHME ME CH2NHME NO2 ME CH2NHME ME H CH2Ph Et Et CH2Ph OH Et CH2Ph Et H CH2Ph nPr NPr CH2Ph NPr H CH2Ph nPr NPr CH2Ph NPr NPr CH2Ph nPr NPr H CH2Ph nPr NPr CH2Ph nPr H H		iPr	Н	nPr	iPr '	NHMs	nPr	iPr	nPr	NHMs
tBu H Ph tBu CHO Ph tBu Ph H Ph CI Et Ph SO ₃ H Et Ph Et H CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr H CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI CI CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph CH ₂ NH ₂ Ph H CH ₂ NHMe Me Me CH ₂ NHMe NO ₂ Me CH ₂ NHMe Me H CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph nPr H		nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
Ph CI Et Ph SO ₃ H Et Ph Et H CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr H CH ₂ OH CI Ph CH ₂ OH OH Ph CH ₂ OH Ph H CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI CI CH ₂ OMe nPr CI CH ₂ OMe COOH CI CH ₂ OMe CI CI CH ₂ NH ₂ Ph CI CH ₂ NH ₂ CONH ₂ CI CH ₂ NH ₂ CI CI CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHME Et CH ₂ NH ₂ Et H CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMS nPr CH ₂ NH ₂ nPr H CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMS Ph CH ₂ NH ₂ Ph H CH ₂ NHME ME ME CH ₂ NHME NO ₂ ME CH ₂ NHME ME H CH ₂ Ph nPr CH ₂ Ph OH Et CH ₂ Ph nPr H		nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
CH2OH CI nPr CH2OH SO2NHMe nPr CH2OH nPr H CH2OH CI Ph CH2OH OH Ph CH2OH Ph H CH2OMe Et CI CH2OMe COMe CI CH2OMe CI CI CH2OMe nPr CI CH2OMe COOH CI CH2OMe CI CI CH2NH2 Ph CI CH2NH2 CONH2 CI CH2NH2 CI CI CH2NH2 H Et CH2NH2 CONHME Et CH2NH2 Et H CH2NH2 H nPr CH2NH2 CONHMS nPr CH2NH2 nPr H CH2NH2 H Ph CH2NH2 NHMS Ph CH2NH2 Ph H CH2NH4 H Ph CH2NH4 NO2 Me CH2NHME ME H CH2Ph Et Et CH2Ph OH Et CH2Ph nPr H		tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Ph	CI	Et 🕔	Ph	SO₃H	Et	Ph	Et	Н
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		CH ₂ OH	CI	Ph		ОН	Ph	CH ₂ OH	Ph	Н
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH $_2$ NHMe Me Me CH $_2$ NHMe NO $_2$ Me CH $_2$ NHMe Me H CH $_2$ Ph Et Et CH $_2$ Ph OH Et CH $_2$ Ph Et H CH $_2$ Ph nPr nPr CH $_2$ Ph COMe nPr CH $_2$ Ph nPr H	(CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH $_2$ NHMe Me Me CH $_2$ NHMe NO $_2$ Me CH $_2$ NHMe Me H CH $_2$ Ph Et Et CH $_2$ Ph OH Et CH $_2$ Ph Et H CH $_2$ Ph nPr nPr CH $_2$ Ph COMe nPr CH $_2$ Ph nPr H	(CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
$\mathrm{CH_2Ph}$ Et Et $\mathrm{CH_2Ph}$ OH Et $\mathrm{CH_2Ph}$ nPr nPr $\mathrm{CH_2Ph}$ nPr H			Ме	Me		NO_2	Ме	CH ₂ NHMe	Ме	Н
CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr H		_	Et	Et	CH₂Ph	ОН	' Εt	CH ₂ Ph	Et	H
-		_	nPr	nPr	_	COMe	nPr	CH ₂ Ph	nPr	Н
	С	H ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	· R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	H	Н	NO ₂
Н	Н	iPr	Н	CHO	H	H	Н	CHO
Н	H	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	H	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	H	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Εt	Ph	Н	Εt	CONH ₂	Н	Et	Н	CONH ₂
Εt	Н	Et	Et	CONHMe	Εt	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	· nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et 、	Ph	SO₃H	Εt	Ph	Εt	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH ₂ NH ₂	Εt	Н
CH ₂ NH ₂	Н	nPr	CH_2NH_2	CONHMs	nPr	CH_2NH_2	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Ме	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph	CH ₂ CH ₂ Ph	Ph	Н
	-,							

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
<u></u>	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	H	Н	CHO
·· H	Н	nPr	Н	SO₃H	.H	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Н	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Ме	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Εt	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO ₂	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et 、	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	OH [°]	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	Cl	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	H	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH_2NH_2	Ph	Н
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Me	CH₂NHMe	Ме	Н
⊂ CH₂Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ Ph	Ph ·	H
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HN-Me	HN	HN	HN
HN-Et	HN	HN	HN
HN		ÓH	^ ^ ^
HN ·	HN	HN	HN
HN	HN	HNOO	HN F
HN	HN	HN	HN
HN	HN		Me
HN	,	HN	HN
HN	HN	HN	HN
HN	HN	HN O	
HN	HN	HN	HN
HN	HN	HN N H	HN
HNOH		HN	HN
HNO	HN		~ ~0

HN-R

HN-R

HN-R

HN-R

HN-R

	HN-Me	HN	HN HN
	HN-Et	HN	HN HN
	HN		ÖH
	HN	HN	HN
	HN	HN	HN HN F
	HN	HN	HN
	HN	HN .	F Me
٠	HN		HN HN N
	HN	HN	HN HN
	HN	HN	HN
	HN	HN	HN
	HN	HN	HN N HN S
	HN OH	HN	HN O HN O
	.		

HN-R

HN SO ₃ H	HNOEt	Me HN Me
H ₂ NO ₂ S	MeOCO	OMe
CH ₂ OH	NHCOOEt	HNOMe
HN	HN	OMe
COCH ₃	HN	OMe
CI	HN OCOCH3	HN NO ₂
HN	Me OH HN	OMe
HN O	OH Me	HN NHCOPh Br
HN	OH Br	HN

Н	N	—	R

HNMe	HN	HN HN
HNEt	HN	HN HN
HN		ÓH
HN	HN	HN
HN	HN	HN HN F
HN	HN	HN HN
HN	HN	F Me
HN	,	HN HN
HN	HN	HN S
HN	HN	HN
HN	HN	HN HN
HN	HN	HN N HN S
HNOH	î	$HN \longrightarrow O \longrightarrow HN \longrightarrow O \longrightarrow O$
HN	HN V	

HN-R

HN-R

HN-R

HN-Me	HN	HN HN
HN-Et	HN	HN HN
HN		ÓН
HN	HN	HN
HN	HN	HN HN F
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HN	HN	F .
HN	niv ·	HN HN N
HN	HN	HN S HN
HN	HN	HN
HN	HN	HN
HN	HN	$HN \longrightarrow N$ H $HN \longrightarrow S$
HNOH		HN O HN O
HN	HN	0

HN-R

HN-R

HN SO ₃ H	OMe	Me HN Me
H ₂ NO ₂ S	MeOCO	OMe
CH ₂ OH	NHCOOEt	HNOMe
COCH ₃	HN	HNOMe
CI	HN OCOCH ₃	HN CO ₂ H
HN	Me OH	OMe
	OH Me	NHCOPh Br
HN	OH Br	HN N H

HN-R

HN-R

HN	_P

1114 11			
HN-Me	HN	HN	HN
HNEt	HN	HN	HN
HN		ÓН	
HN	HN	HN	HN
HN	HN	HN O	HN
HN	HN	HN	HN
HN	HN		F
HN	,	HN	Me N N
HN	HN	HN	HN
HN	HN	HN O	
HN	HN	HN	HN V
HN	HN	HN N H	HN
HNOH		HN O	HN
HN	HN		0

HN-R

HN-R

HN SO ₃ H	OMe	Me HN Me
H ₂ NO ₂ S	MeOCO	OMe
CH₂OH	NHCOOEt	HNOMe
HN	HN	OMe
COCH ₃	HN OPh	HNOMe
	OCOCH3	HN NO ₂
HN	Me OH	OMe
HÍN O	OH Me HN	HN Br
HN	OH Br	HN N H

HN-R

rin-rx			
HN	HN	HN	HN
HN N-N	HN	HN	HN
HN N	HN	HN	HN N
HN N	HN N	HN	HŅ —
HN N CI	HN CI	HN	HN
N		N O	HN
HN N	HN N	L N	$HN \longrightarrow N$
HN	HN	HN N-S	
HN	HN N H	HN N-S	HN
HN	HN	HN S	HN O H

Н	N	_	P

HN-Me	HN	HN HN	
HN-Et	HN	HN HN	
HN		ÓН	
HN	HN	HN HN	F
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HN	HN	HN HN N	
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HNOH		HN O HN	.0
HN	HN HN		

HN-R

HN-R

HN-R

Н	N	_	R

HN-Me	HN	HN	HN
HN-Et	HN	HN	HN
HN		ОН	
HN	HN	HN	HN
HN	HN	HNO	HN
HN	HN	HN	HN
HN			F
HN	HN	HN	HN N
HN	HN	HN	HN
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HN	HN	HN	HN
HN	HN	HN N H	HN
HNOH		HN	HN
HN	HN		✓ → 0

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S N O Me Me

HN-R

HN-R

HN-R

THN IX		i.	
HN	HN	HN	HN
HN N-N	HN	HN	HN
HN N	HN	HN	HN N
HN N	HN N	HN	
N CI	HN CI	HN NH	HN
N √ N ✓ OI		N	HN N
HN N	HN N H		HN
HN N	HN	HN N-S	Ö
HN	HN N H	HN N-S	HN N
HN	HN	$-HN \longrightarrow N$	HN N N

HN-R

HN	HNOH	HN	HN
HN	HN	HN	HN ON N
HN	HN	HN	F HN N
HN	HN	HN	HN
HN	HN	2 HN F	HN O
HN	HN	HN COOH	HN
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN	HN	HN	HN N CI
HNOH	HN		HN N
HN	HN	HN OH	

HN-R

HN-R

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HN	HN	HN	$HN \longrightarrow N$
HN	ÓН	LINI	o N
HN	HN F	HN	HN N
HN	HN:	HN	F HN N
	HN	HN	HN
HN	NH	2	HN
HN	HN F.	HN F	HN O
HN \	HN	ни соон	HN
HN	HN OH	HN NH ₂	HN
HN	HNO	HN	HN
HN	HN	HN Me	HN N CI
HNOH	HN		HN N
HN O	HN	HN OH .	

HN-R

HN ~	HN OH	HN	$HN \longrightarrow N$
HN	HN	HN	HN
HN	HN	HN	F HN N
HN	HN	HN	HN
HN	HN	HN F	HN O
HN	HN	HN COOH	HN
HN	HNOH	HN NH ₂	HN
HN	HN	HN HN Me	HN
HN	HN	HN	HN N CI
HNOH	HN		HN N
HNOO	HN	HN OH .	

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н .	Н	NO ₂
H	Н	iPr	Н	CHO	Н	Н	Н	CHO
H	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
H	Н	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	H	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	H	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Εt	Н	Et	Εt	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu⊸	nBu	NO ₂	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Εt	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	OH	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	Cl	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Η	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH₂NHMe	Ме	Ме	CH ₂ NHMe	NO ₂	Ме	CH ₂ NHMe	e Me	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	ńΡr	nPr	CH ₂ Ph	COMe	nPr ·	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH_2CH_2Ph	COOH	Ph	CH ₂ CH ₂ Pł	ר Ph	Н
			•					

					1710				
	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	· R ¹³	R ¹⁴
	Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
	Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
	Н	Н	nPr	Н	SO ₃ H	Н	Н	Н	SO₃H
	Н	Н	nBu	H	CI	Н	Н	Н	CI
	Н	Н	tBu	Н	Br	Н	Н	Н	Br
	Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
	Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
	Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
	Me	nPr	Н	Me	CH ₂ Ph	H	Me	Н	CH ₂ Ph
	Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
	Me	tBu	Н	Me	COOH	Н	Ме	Н	COOH
	Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
	Et	Н	Et	Εt	CONHMe	Et	Et	Et	CONHMe
	Et	Н	iPr	Εt	CONHMs	iPr	Et ,	iPr	CONHMs
	iPr	Н	nPr	iPr	NHMs	· nPr	iPr	nPr	NHMs
	nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
	nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
	tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
	Ph	CI	Et 、	Ph	SO₃H	Et	Ph	Et	Н
	CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
	CH ₂ OH	CI	Ph	CH ₂ OH	OH	Ph	CH ₂ OH	Ph	Н
	CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe		CI
	CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe		CI
	CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
	CH ₂ NH ₂	Н	Et	CH_2NH_2	CONHMe	Et	CH ₂ NH ₂	Et	Н
	CH ₂ NH ₂	Н	nPr	CH_2NH_2	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
	CH ₂ NH ₂	Н	Ph	CH_2NH_2	NHMs	Ph	CH ₂ NH ₂		Н
(CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Me	CH ₂ NHMe	e Me	Н
	CH ₂ Ph	Εt	Et	CH ₂ Ph	ОН	Εt	CH₂Ph	Et	Н
	CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
C	H ₂ CH ₂ Ph	Ph ·	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH ₂ CH ₂ PI	h Ph	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	H	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	H	SO₃H
Н	H	nBu	Н	CI	Н	H	Н	CI
Н	Н	tBu	Н	Br	Н	Н	H	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	H	CH ₂ OH
Me	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	H	CH_2NH_2
Me ·	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Εt	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	· nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	. Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr ,	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	H
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph ——	CH ₂ CH ₂ Ph	Ph	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	H	nBu	Н	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	H	Ph	Me	CH ₂ OH	Н	Ме	Н	CH ₂ OH
Ме	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Ме	tBu	H	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Εt	CONH ₂	Н	Et	Н	CONH ₂
Εt	Н	Et	Et	CONHMe	Εt	Et	Εt	CONHMe
Εt	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO ₂	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Εt	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH₂OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH₂OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Εt	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Εt	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH ₂ Ph	Et	Et	CH₂Ph	OH	Et	CH₂Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
H ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph	CH ₂ CH ₂ Ph	Ρḥ	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	H	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	H	CI	Н	Н	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	H	Me	Н	CH ₂ OH
Ме	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et	Et	Εt	CONHMe
Et	Н	iPr	Et	CONHMs	[·] iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu _.	tBu	NO_2
tBu	Н	Ph 1	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO₃H	Et	Ph	Εt	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	Cl	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPŗ	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Εt	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Η	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Ме	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	OH	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ρh	Ph	CH ₂ CH ₂ Ph	СООН	Ph·	CH ₂ CH ₂ Ph	Ph	H
								

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	_	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н		Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н		H	H	CHO
Н	Н	nPr	Н	SO₃H	Н		Н	Н	SO₃H
Н	Н	nBu	Н	CI	H		Н	Н	CI
Н	Н	tBu	Н	Br	Н		Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	H		Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н		Ме	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н		Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н		Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н		Me	H	COMe
Me	tBu	Н	Me	COOH	Н		Me	Н	COOH
Εt	Ph	Н	Et	CONH ₂	Н		Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et		Et	Et	CONHMe
Et	Н	iPr	Et	CONHMs	iPr		Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr		iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu		nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu		nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph		tBu	Ph	Н
Ph	CI	Et '	Ph	SO₃H	Εt		Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	С	H ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	С	H ₂ OH	Ph	Н
CH₂OMe	Et	CI	CH ₂ OMe	COMe	CI	CI	H₂OMe	CI	CI
CH ₂ OMe	nPr	Cl	CH ₂ OMe	COOH	CI	Cl	_{d₂} OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	С	H_2NH_2	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	C	H_2NH_2	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	C	H_2NH_2	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	C	H_2NH_2	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH	l ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Et	CH ₂ Ph	OH	Εt	C	H ₂ Ph	Εt	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	C	H ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph	CH	₂ CH ₂ Ph	Рh	Н
					-				

R11 R13 R14 R11 R13 R14 R11 R13 R14 R11 R13 H	R ¹⁴ NO ₂ CHO SO ₃ H CI Br CH ₂ OH CH ₂ NH ₂ CH ₂ NHMe CH ₂ Ph COMe COOH
H H H iPr H CHO H H H H H NPr H SO ₃ H H H H H H NBu H CI H Me H Ph Me CH ₂ OH H Me H Me iPr H Me CH ₂ NHMe H Me H Me iPr H Me CH ₂ NHMe H Me H Me nPr H Me COMe H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et Et Et H iPr Et CONHMe iPr iPr nPr nPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO ₂ tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO ₃ H Et Ph Et	CHO SO ₃ H CI Br CH ₂ OH CH ₂ NH ₂ CH ₂ NHMe CH ₂ Ph COMe COOH
H H nPr H SO ₃ H M H H M H M H H M H H M H H M H H M H H M H H M H H M H H M H M H M H M H M H H M H M H H M H M H<	SO_3H CI Br CH_2OH CH_2NH_2 CH_2Ph $COMe$
H H H tBu H Br H H H H H H H H H H H H H H H H H	CI Br CH ₂ OH CH ₂ NH ₂ CH ₂ NHMe CH ₂ Ph COMe COOH
H H tBu H Br H H H Me H Ph Me CH ₂ OH H Me H Me Et Ph Me CH ₂ NH ₂ H Me H Me iPr H Me CH ₂ NHMe H Me H Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et Et Et H iPr Et CONHMe iPr iPr nPr nPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO ₂ tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO ₃ H Et Ph Et CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	${ m Br}$ ${ m CH_2OH}$ ${ m CH_2NH_2}$ ${ m CH_2NHMe}$ ${ m CH_2Ph}$ ${ m COMe}$ ${ m COOH}$
Me H Ph Me CH ₂ OH H Me H Me Et Ph Me CH ₂ NH ₂ H Me H Me iPr H Me CH ₂ NHMe H Me H Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHME Et	${ m CH_2OH}$ ${ m CH_2NH_2}$ ${ m CH_2NHMe}$ ${ m CH_2Ph}$ ${ m COMe}$ ${ m COOH}$
Me Et Ph Me CH2NH2 H Me H Me iPr H Me CH2NHME H Me H Me nPr H Me CH2Ph H Me H Me nBu H Me COME H ME H Me tBu H Me COOH H ME H Et Ph H Et CONH2 H Et H Et H Et Et CONHME Et Et Et Et H iPr Et CONHMS iPr Et iPr iPr H nPr iPr NHMS nPr iPr nPr nPr H nBu nPr NHCOME nBu nPr nBu nBu H tBu nBu NO2 tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO3H Et Ph Et CH2OH CI nPr CH2OH SO2NHME nPr CH2OH nPr	${ m CH_2NH_2}$ ${ m CH_2NHMe}$ ${ m CH_2Ph}$ ${ m COMe}$ ${ m COOH}$
Me iPr H Me CH_2NHMe H Me H Me Me Me nPr H Me CH_2Ph H Me H Me CH_2Ph H Me H Me $COMe$ H Me H Me H Me $COMe$ H Me H Me H Me H Me $COMe$ H Me H	CH ₂ NHMe CH ₂ Ph COMe COOH
Me nPr H Me CH ₂ Ph H Me H Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et Et H iPr Et CONHMs iPr Et iPr iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO ₂ tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO ₃ H Et Ph Et CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	CH ₂ Ph COMe COOH
Me nBu H Me COMe H Me H Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHME Et Et Et Et H iPr Et CONHMS iPr Et iPr iPr H nPr iPr NHMS nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO ₂ tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO ₃ H Et Ph Et CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	COMe COOH
Me tBu H Me COOH H Me H Et Ph H Et CONH ₂ H Et H Et H Et Et CONHMe Et Et Et Et H iPr Et CONHMs iPr Et iPr iPr H nPr iPr NHMs nPr iPr nPr nPr H nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO ₂ tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO ₃ H Et Ph Et CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	COOH
Et Ph H Et CONH ₂ H Et CONHMe Et Et Et Et Et Et H iPr Et CONHMs iPr Et iPr iPr H nPr iPr NHMs nPr iPr nPr nPr nPr h nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO ₂ tBu nBu tBu tBu H Ph TBu CHO Ph TBu Ph CI Et Ph SO ₃ H Et Ph Et CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	
Et H Et Et CONHMe Et Et Et Et Et Et Et H iPr Et CONHMs iPr Et iPr iPr H nPr iPr NHMs nPr iPr nPr nPr nPr hBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO2 tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO3H Et Ph Et CH2OH CI nPr CH2OH SO2NHMe nPr CH2OH nPr	CONH ₂
Et H iPr Et CONHMs iPr Et iPr iPr H nPr iPr NHMs nPr iPr nPr nPr nPr nPr nPr nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO2 tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO3H Et Ph Et CH2OH CI nPr CH2OH SO2NHMe nPr CH2OH nPr	2
iPr H nPr iPr NHMs nPr iPr nPr nPr nPr h nBu nPr NHCOMe nBu nPr nBu nBu nBu tBu nBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO ₃ H Et Ph Et CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	CONHMe
nPr H nBu nPr NHCOMe nBu nPr nBu nBu H tBu nBu NO $_2$ tBu nBu tBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO $_3$ H Et Ph Et CH $_2$ OH CI nPr CH $_2$ OH SO $_2$ NHMe nPr CH $_2$ OH nPr	CONHMs
nBu H tBu nBu NO $_2$ tBu nBu tBu tBu tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO $_3$ H Et Ph Et CH $_2$ OH CI nPr CH $_2$ OH SO $_2$ NHMe nPr CH $_2$ OH nPr	NHMs
tBu H Ph tBu CHO Ph tBu Ph Ph CI Et Ph SO $_3$ H Et Ph Et CH $_2$ OH CI nPr CH $_2$ OH SO $_2$ NHMe nPr CH $_2$ OH nPr	NHCOMe
Ph CI Et Ph $\mathrm{SO_3H}$ Et Ph Et CH2OH CI nPr CH2OH $\mathrm{SO_2NHMe}$ nPr CH2OH nPr	NO_2
CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr CH ₂ OH nPr	Н
_	Н
CH_OH CI Ph CH_OH OH Ph CH_OH Ph	Н
	Н
CH ₂ OMe Et CI CH ₂ OMe COMe CI CH ₂ OMe CI	CI
CH ₂ OMe nPr Cl CH ₂ OMe COOH Cl CH ₂ OMe Cl	CI
CH ₂ NH ₂ Ph Cl CH ₂ NH ₂ CONH ₂ Cl CH ₂ NH ₂ Cl	CI
CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et CH ₂ NH ₂ Et	Н
CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr CH ₂ NH ₂ nPr	Н
CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph CH ₂ NH ₂ Ph	Н
CH ₂ NHMe Me CH ₂ NHMe NO ₂ Me CH ₂ NHMe Me	Н
CH ₂ Ph Et Et CH ₂ Ph OH Et CH ₂ Ph Et	Н
CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr CH ₂ Ph nPr	Н
CH ₂ CH ₂ Ph Ph Ph CH ₂ CH ₂ Ph COOH Ph CH ₂ CH ₂ Ph Ph	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	['] R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	H	CHO.	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	H	CI	Н	H	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	H	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHM
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	H	CH ₂ Ph
Ме	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	H	Et	Н	CONH ₂
Et	Н	Εt	Εt	CONHMe	Et	Et	Et	CONHM
Et	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMS
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOM
nBu	Н	tBu	nBu	NO ₂	tBu	nBu	tBu	NO_2
tBu	Н	Ph	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et '	Ph	SO₃H	Et	Ph	Εt	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Ме	CH₂NHMe	Ме	Н
CH ₂ Ph	Εt	Et	- CH₂Ph	ОH	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	H
CH ₂ CH ₂ Ph	Ph	· Ph	CH ₂ CH ₂ Ph	COOH	Ph	CH ₂ CH ₂ Ph	Ph	Н

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴		R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	H		Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н		Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н		Н	Н	SO₃H
Н	Н	nBu	Η.	CI	Н		Н	Н	CI
Н	Н	tBu	Н	Br	Н		Н	Н	Br
Me	Н	Ph	Ме	CH ₂ OH	Н		Ме	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н		Ме	Н	CH ₂ NH ₂
Me	iPr	Н	Ме	CH ₂ NHMe	Н		Ме	H	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	:	Ме	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н		Ме	Н	COMe
Me	tBu	Н	Me	COOH	Н		Мe	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н		Et	Н	CONH ₂
Et	Н	Et	Et	CONHMe	Et		Et	Et	CONHMe
Et	Η	iPr	Εt	CONHMs	iPr		Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr		iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	1	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO ₂	tBu	r	nBu	tBu	NO_2
tBu	Н	Ph 、	tBu	CHO	Ph	· t	tBu	Ph	Н
Ph	CI	Et	Ph	SO ₃ H	Et		Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH	d₂OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH	H₂OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	СН	₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH	₂ OMe	CI	CI
CH ₂ NH ₂	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH	I_2NH_2	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH	I_2NH_2	Et	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH	I_2NH_2	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH	I_2NH_2	Ph	Н
CH₂NHMe	Ме	Ме	CH ₂ NHMe	NO_2	Me	CH ₂	NHMe	Me	Н
CḤ ₂ Ph	Et	Et	CH ₂ Ph	OH	Εt	CH	H₂Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr		₁ ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	COOH	Ph ·	CH ₂	CH ₂ Ph	Ρĥ	H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	Н	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	Н	CHO
Н	Н	nPr	Н	SO₃H	Н	Н	Н	SO₃H
Н	Н	nBu	Н	CI	Н	H	H	Cl
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	Н	Me	Н	CH ₂ OH
Me	Et	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Ме	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Εt	Ph	Н	Εt	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Εt	Et	CONHMe	Et	Et	Et	CONHMe
Εt	Н	iPr	Et	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO ₂	tBu	nBu	tBu	NO_2
tBu	Н	Ph 、	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Et	Ph	SO ₃ H	Et	Ph	Et	Η .
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Εt	CI	CH ₂ OMe	COMe	CI	· CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH ₂ NH ₂	Ph ·	CI	CH ₂ NH ₂	CONH ₂	CI	CH_2NH_2	CI	CI
CH ₂ NH ₂	Н	Et	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Εt	Н
CH ₂ NH ₂	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH_2NH_2	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Ме	Me	CH ₂ NHMe	NO_2	Ме	CH ₂ NHMe	Me	Н
CḤ ₂ Ph	Et	Et	CH ₂ Ph	ОН	Et	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH ₂ Ph	nPr	Н
CH ₂ CH ₂ Ph	Ph	Ph	CH ₂ CH ₂ Ph	СООН	Ph ·	CH ₂ CH ₂ Ph	Ph	H

R ¹¹ R ¹³ R ¹⁴ R ¹¹ R ¹³ R ¹⁴	R ¹¹ R ¹³ R ¹⁴
	– <u>— </u>
H H Et H NO ₂ H	- · · ·
H H iPr H CHO H	н н сно
H H nPr H SO ₃ H H	H H SO₃H
H H nBu H CI H	H H Cl
H H tBu H Br H	H H Br
Me H Ph Me CH ₂ OH H	Me H CH ₂ OH
Me Et Ph Me CH ₂ NH ₂ H	Me H CH ₂ NH ₂
Me iPr H Me CH ₂ NHMe H	Me H CH ₂ NHM
Me nPr H Me CH ₂ Ph H	Me H CH ₂ Ph
Me nBu H Me COMe H	Me H COMe
Me tBu H Me COOH H	Me H COOH
Et Ph H Et CONH ₂ H	Et H CONH ₂
Et H Et Et CONHMe Et	Et Et CONHM
Et H iPr Et CONHMs iPr	Et iPr CONHM
iPr H nPr iPr NHMs nPr	
nPr H nBu nPr NHCOMe nBu	
nBu H tBu nBu NO ₂ tBu	-
tBu H Ph tBu CHO Ph	tBu Ph H
Ph Cl Et Ph SO ₃ H Et	Ph Et H
CH ₂ OH CI nPr CH ₂ OH SO ₂ NHMe nPr	
CH ₂ OH CI Ph CH ₂ OH OH Ph	CH ₂ OH Ph H
CH ₂ OMe Et Cl CH ₂ OMe COMe Cl	CH ₂ OMe CI CI
CH ₂ OMe nPr Cl CH ₂ OMe COOH Cl	CH ₂ OMe CI CI
CH ₂ NH ₂ Ph Cl CH ₂ NH ₂ CONH ₂ Cl	CH ₂ NH ₂ CI CI
CH ₂ NH ₂ H Et CH ₂ NH ₂ CONHMe Et	CH ₂ NH ₂ Et H
CH ₂ NH ₂ H nPr CH ₂ NH ₂ CONHMs nPr	
CH ₂ NH ₂ H Ph CH ₂ NH ₂ NHMs Ph	CH ₂ NH ₂ Ph H
CH ₂ NHMe Me CH ₂ NHMe NO ₂ Me	CH₂NHMe Me H
CH ₂ Ph Et Et CH ₂ Ph OH Et	CH₂Ph Et H
CH ₂ Ph nPr nPr CH ₂ Ph COMe nPr	
CH ₂ CH ₂ Ph Ph Ph CH ₂ CH ₂ Ph COOH Ph	CH ₂ CH ₂ Ph Ph H

R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴	R ¹¹	R ¹³	R ¹⁴
Н	Н	Et	. H	NO ₂	Н	Н	Н	NO ₂
Н	Н	iPr	Н	CHO	Н	Н	H	CHO
Н	Н	nPr	Н	SO₃H	Н	H	Н	SO ₃ H
Н	Н	nBu	Н	CI	Н	H	Н	CI
Н	Н	tBu	Н	Br	Н	Н	Н	Br
Me	Н	Ph	Me	CH ₂ OH	H	Me	Н	CH ₂ OH
Me	Εt	Ph	Me	CH ₂ NH ₂	Н	Me	Н	CH ₂ NH ₂
Me	iPr	Н	Me	CH ₂ NHMe	Н	Me	Н	CH ₂ NHMe
Me	nPr	Н	Me	CH ₂ Ph	Н	Me	Н	CH ₂ Ph
Me	nBu	Н	Me	COMe	Н	Me	Н	COMe
Me	tBu	Н	Me	COOH	Н	Me	Н	COOH
Et	Ph	Н	Et	CONH ₂	Н	Et	Н	CONH ₂
Et	Н	Et	Εt	CONHMe	Et	Et	Et	CONHMe
Et	Н	iPr	Εt	CONHMs	iPr	Et	iPr	CONHMs
iPr	Н	nPr	iPr	NHMs	nPr	iPr	nPr	NHMs
nPr	Н	nBu	nPr	NHCOMe	nBu	nPr	nBu	NHCOMe
nBu	Н	tBu	nBu	NO_2	tBu	nBu	tBu	NO_2
tBu	Н	Ph v	tBu	CHO	Ph	tBu	Ph	Н
Ph	CI	Εt	Ph	SO₃H	Et	Ph	Et	Н
CH ₂ OH	CI	nPr	CH ₂ OH	SO ₂ NHMe	nPr	CH ₂ OH	nPr	Н
CH ₂ OH	CI	Ph	CH ₂ OH	ОН	Ph	CH ₂ OH	Ph	Н
CH ₂ OMe	Et	CI	CH ₂ OMe	COMe	CI	CH ₂ OMe	CI	CI
CH ₂ OMe	nPr	CI	CH ₂ OMe	COOH	CI	CH ₂ OMe	CI	CI
CH_2NH_2	Ph	CI	CH ₂ NH ₂	CONH ₂	CI	CH ₂ NH ₂	CI	CI
CH ₂ NH ₂	Н	Εt	CH ₂ NH ₂	CONHMe	Et	CH ₂ NH ₂	Et	Н
CH_2NH_2	Н	nPr	CH ₂ NH ₂	CONHMs	nPr	CH ₂ NH ₂	nPr	Н
CH ₂ NH ₂	Н	Ph	CH ₂ NH ₂	NHMs	Ph	CH ₂ NH ₂	Ph	Н
CH ₂ NHMe	Me	Me	CH ₂ NHMe	NO_2	Me	CH ₂ NHMe	Ме	Н
CH ₂ Ph	Et	Εt	CH ₂ Ph	ОН	Εt	CH ₂ Ph	Et	Н
CH ₂ Ph	nPr	nPr	CH ₂ Ph	COMe	nPr	CH₂Ph	nPr	Н
CH ₂ CH ₂ Ph	·Ph	Ph 	CH ₂ CH ₂ Ph	СООН	Ph·	CH ₂ CH ₂ Ph	Ph	H

HN-R

The compound according to the present invention has asymmetric carbon atoms at 3-position and 4-position, thus optical isomers thereof based on the asymmetric carbon atoms are present, and optical active substances can be also used in the application of the present invention, like racemic modifications. Further, cis- and trans-isomer based on configuration at 3-position and 4-position may be included, but trans-isomer is preferred.

Further, when the compounds can form their salts, the pharmaceutically acceptable salts thereof can also be used as active ingredients.

Examples of pharmaceutically acceptable salt are such as hydrochlorides, hydrobromides, sulfates, methanesulfonates, acetates, benzoates, tartrates, phosphates, lactates, maleates, fumarates, malates, gluconates, salicylates and the like.

Preferably, hydrochlorides, maleates and methanesulfonates may be mentioned.

The compound of formula (I-a) or (II-a) that is the compound of formula (I) or (II) wherein R⁴ is hydrogen atom and R³ is hydroxy group can be obtained by reacting the compound of formula (1) or (2) with the compound of formula (3) in an inert solvent as shown in the scheme below.

O R²

$$R^2$$
 R^2
 R^3
 R^4
 R^5
 R^5
 R^4
 R^5
 R^5
 R^5
 R^6
 R^6
 R^7
 R^7

As the solvents used in the reaction of the compound of formula (1) or (2) with the compound of formula (3), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type

solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents and alcohol type solvents may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 100°C.

The molar ratio of the reaction materials is within the range of 0.5-4.0, preferably 1.0-2.0, for compound (3)/compound (1) or (2).

Acid catalysts may be used in the reaction.

The acid catalysts used include inorganic acids exemplified by hydrochloric acid and sulfuric acid, Lewis acids exemplified by aluminum chloride, titanium tetrachloride, boron trifluoride diethylether complex, perchloric acid, lithium perchlorate, lithium bromide and ytterbium trifluoromethanesulfonate.

Preferable acid catalysts are lithium bromide and lithium perchlorate.

The synthesis of optically active compounds in the compounds of formula (I) or (II) is accomplished by use of a method for optical resolution of racemate (Japanese Patent Laid-open No. Hei 3-141286, US Patent No. 5097037 and EP Patent No. 409165).

In addition, the synthesis of the compound of formula (1) or (2) is accomplished by use of the following synthetic process:

- General synthetic process of benzopyran ring

The benzopyran ring can be synthesized according to known methods (methods described in J. M. Evans et al., J. Med. Chem. 1984, 27, 1127; J. Med. Chem. 1986, 29, 2194; J. T. North et al., J. Org. Chem. 1995, 60, 3397; as well as Japanese Patent Laid-open Nos. Sho 56-57785, Sho 56-57786, Sho 58-188880, Hei 2-141, Hei 10-87650 and Hei 11-209366 and the like.);

- Indole or oxyindole
- T. Sakamoto, et al., Heterocycles, 1986, 24, 31,
- M. Belley, et.al., Synthesis, 2001, 222,
- A.D. Cross, et al., J. Chem. Soc., 1961, 2714;
- Imidazolinone
- J. Kitteringham, et.al., Synthetic Commun., 2000, 30, 1937;
- Quinoline

- S. Imor, et al., Synthetic Commun., 1996, 26, 2197,
- Y. Kitahara, et al., Tetrahedron, 1997, 53, 6001,
- A.G. Osborne, et al., J. Chem. Soc. Perkin Trans. 1, 1993, 181,
- R. T. Shuman, et al., J. Org. Chem., 1990, 55, 738,
- T. Sakamoto, et al., Chem. Pharm. Bull., 1981, 29, 2485,
- Y. Tsuji, et al., J. Org. Chem., 1987,52, 1673,
- Z. Song, et al., J. Heterocyclic Chem., 1993, 30, 17;
- Quinolinone
- M.R. Sabol, et al., Synthetic Commun., 2000, 30, 427,
- Z-Y. Yang, et al., Tetrahedron Lett., 1999, 40, 4505,
- H-B Sun, et al., Synthesis, 1997, 1249,
- A. Guiotto, et al., J. Heterocyclic Chem. 1989, 26, 917,
- K. Konno, et al., Heterocycles 1986, 24, 2169,
- E. Fernandez, et al., Synthesis 1995, 1362;
- Benzothiazole or triazole
- N.B.Ambati, et al., Synthetic Commun., 1997, 27, 1487,
- D.E. Burton., et al., J. Chem. Soc (C). 1968, 1268;
- Quinoxaline or quinoxalinone
- J.H. Liu, et al., J. Org. Chem., 2000, 65, 3395,
- J.J.Li, et al., Tetrahedron Lett., 1999, 40, 4507,
- Y.Ahmed, et al., Bull. Chem. Soc. Jpn., 1987, 60, 1145;
- Benzoaxadinone
- G.H.Jones, et al., J. Med. Chem., 1987, 30, 295,
- J.L. Wright, et al., J. Med. Chem., 2000, 43, 3408,
- M.Kluge, et al., J. Heterocyclic Chem., 1995, 32, 395.

The compound of formula (1-a) or (2-a) that is the compound of formula (I) or (II) wherein A is the group of formula (5), R⁴ is hydrogen atom and R³ is hydroxy group can be obtained from the compound of formula (6) or (7) according to known methods (methods described in J. M. Evans et al., J. Med. Chem. 1984, 27, 1127; J. Med. Chem. 1986, 29, 2194; J. T. North et al., J. Org. Chem. 1995, 60, 3397; as well as Japanese Patent Laid-open Nos. Sho 56-57785, Sho 56-57786, Sho 58-188880, Hei 2-141, Hei 10-87650 and Hei 11-209366 and the like).

The compound of formula (6) or (7) can be obtained by reacting compound (8) with compound (9) (see, Y. Tsuji et al., J. Org. Chem., 1987, 52, 1673).

As the solvents used in the reaction of the compound of formula (8) with the compound of formula (9), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran, dioxane and diethylene glycol dimethyl ether; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents and alcohol type solvents may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 200°C.

The molar ratio of the reaction materials is within the range of 0.1-4.0, preferably 0.5-2.0, for compound (8)/compound (9).

Transition metal catalysts and ligands may be used in the reaction.

The transition metal catalysts used include ruthenium chloride, dichlorotris(triphenylphosphine)ruthenium, dibromotris(triphenylphosphine)ruthenium, dihydridetetrakis(triphenylphosphine)ruthenium,

(η 4-cyclooctadiene)(η 6-cyclooctatriene)ruthenium, dichlorotricarbonyl ruthenium dimer, dodecacarbonyl triruthenuim,

(η 5-pentamethylcyclopentadienyl)chloro(η 4-cyclooctatriene)ruthenium, palladium acetate, palladium chloride, dichlorobis(triphenylphosphine)palladium, tetrakistriphenylphosphine palladium, bis(dibenzylideneacetone)palladium, rhodium chloride, chlorotris(triphenylphosphine)rhodium,

hydridecarbonyltristriphenylphosphine rhodium,

hydridetris(triphenylphosphine)rhodium, di- μ -chlorotetracarbonyl dirhodium, chlorocarbonylbis(triphenylphosphine)iridium,

(η 5-pentamethylcyclopentadienyl)dichloroiridium dimer, nickeltetrakistriphenylphosphine, dicobaltoctacarbonyl, (η 5-cycloopentadienyl)dicarbonylcobalt, and the like.

Preferably, ruthenium chloride may be mentioned.

The ligands include monodentate phosphine ligands exemplified by trimethylphosphine, triethylphosphine, tri-*n*-propylphosphine, tri-*i*-propylphosphine, tri-*n*-butylphosphine, tri-*t*-butylphosphine, tricyclohexylphosphine, triphenylphosphine and tri(*o*-tolyl)phosphine, bidentate phosphine ligands exemplified by 1,2-bisdiphenylphosphinoethane, 1,3-bisdiphenylphosphinopropane,

1,4-bisdiphenylphosphinobutane and 1,2-diethylphosphinoethane, phosphite ligands exemplified by triethylphosphite, tributylphosphite, triphenylphosphite and tri(o-tolyl)phosphite.

Preferably, triphenylphosphine, tri-*n*-butylphosphine and tri-*t*-butylphosphine.

The compound of formula (6) or (7) can be also obtained by reacting compound (8) with compound (10) in the presence of an acid catalyst (see, Y. Kitahara et al., Tetrahedron Lett., 1997, 53, 6001, Z. Song et al., J. Heterocyclic Chem., 1993, 30, 17).

$$H_2N$$
 R^{13}
 R^{15}
 R^{15}
 R^{14}
 R^{15}
 R^{14}
 R^{15}
 R^{15}
 R^{14}
 R^{15}
 R^{15}
 R^{14}
 R^{15}
 $R^{$

As the solvents used in the reaction of the compound of formula (8) with the compound of formula (10), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran, dioxane and diethylene glycol dimethyl ether; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; organic acid type solvents exemplified by acetic acid and trifluoroacetic acid; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents, alcohol type solvents and organic acid type solvents may be mentioned.

The acid catalysts used include inorganic acids exemplified by hydrochloric acid, sulfuric acid, nitric acid and phosphoric acid, organic sulfonic acids exemplified by methane sulfonic acid and paratoluene sulfonic acid, Lewis acids exemplified by aluminum chloride, titanium tetrachloride, boron trifluoride diethylether complex, perchloric acid, zinc chloride, zinc bromide, zinc iodide, iron(III) chloride, iron(III) chloride. copper(I) chloride and copper(II) chloride. Preferably, hydrochloric acid and zinc chloride may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 200°C.

The molar ratio of the reaction materials is within the range of 1-10, preferably 1-3, for compound (10)/compound (8).

Furthermore, syntheses of optically active compounds in the compounds of of formula (1) or (2) can be attained by utilizing asymmetric synthetic methods (PCT

Japanese Translation Patent Publication No. Hei 5-507645, Japanese Patent Laid-open Nos. Hei 5-301878 and Hei 7-285983, European Patent Laid-open No.535377 and U.S. Patent No. 5420314).

The compound of formula (I-a) or (II-a) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom and R^3 is hydroxy group can be obtained by subjecting the compound of formula (11) or (12) and the compound of formula (13) to reductive amination reaction in an inert solvent as shown in the scheme below.

As the solvents used in the reaction of the compound of formula (11) or (12) with the compound of formula (13), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents and alcohol type solvents may be mentioned.

The compound of formula (I-b) or (II-b) that is the compound of formula (I) or (II) wherein R⁴ is hydrogen atom and R³ is hydroxy group, m is 1, V is CR⁷OH can be obtained by reacting the compound of formula (11) or (12) with the compound of formula (14) in an inert solvent as shown in the scheme below.

As the solvents used in the reaction of the compound of formula (11) or (12) with the compound of formula (14), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents, nitrile type solvents and alcohol type solvents may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 100°C.

The molar ratio of the reaction materials is within the range of 0.5-4.0, preferably 1.0-2.0, for compound (14)/compound (11) or (12).

The acid catalysts used include inorganic acids exemplified by hydrochloric acid and sulfuric acid, Lewis acids exemplified by aluminum chloride, titanium tetrachloride, boron trifluoride diethylether complex, perchloric acid, lithium perchlorate, lithium bromide and ytterbium trifluoromethanesulfonate.

Preferable acid catalysts are lithium bromide and lithium perchlorate.

The compound of formula (I-c) or (II-c) that is the compound of formula (I) or (II) wherein R^4 is hydrogen atom, R^3 is hydroxy group and A is the group of formula (15) can be also obtained by reacting the compound of formula (16) or (17) with the

compound of formula (18) in an inert solvent as shown in the scheme below.

As the solvents used in the reaction of the compound of formula (16) or (17) with the compound of formula (18), the followings may be mentioned.

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide and dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran and dioxane; halogen type solvents exemplified by dichloromethane, chloroform and dichloroethane; nitrile type solvents exemplified by acetonitrile and propionitrile; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane and heptane; ester type solvents exemplified by ethyl acetate; alcohol type solvents exemplified by methanol, ethanol, 1-propanol, 2-propanol and ethylene glycol; and water may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, alcohol type solvents may be mentioned.

The reaction temperature is generally from -80°C to the reflux temperature of the reaction solvent, preferably from -10°C to 50°C.

The molar ratio of the reaction materials is within the range of 0.5-4.0, preferably 0.8-2.0, for compound (18)/compound (16) or (17).

The compound of formula (I-d) or (II-d) that is the compound of formula (I) or (II) wherein R⁴ is hydrogen atom, R³ is hydroxy group and A is the group of formula (19) can be also obtained by subjecting the compound of formula (20) or (21) to reduction reaction in an inert solvent as shown in the scheme below.

The compound of formula (I-e) or (II-e) that is the compound of formula (I) or (II) wherein R⁴ is hydrogen atom, R³ is hydroxy group and A is the group of formula (22) (X is SO₂ or CO, and Y is S or O) can be also obtained by subjecting the compound of formula (23) or (24) to ring-closure reaction in an inert solvent under basic conditions as shown in the scheme below.

The compounds of formula (I) or (II) that are not included in the compounds of formula (I-a to I-e) and (II-a to II-e), that is, the compounds of formula (I) or (II) wherein R^3 and R^4 are together a bond, or R^4 is hydrogen atom and R^3 is C_{1-6} alkylcarbonyloxy group, can be produced by a preparation process similarly to that described in Japanese Patent Laid-open Nos. Sho 52-91866 and Hei 10-87650.

As described above, the inventors of the present invention found that the compound of formula (I) or (II) has a strong prolongation effect on the refractory period. The prolongation effect on the refractory period is one of mechanisms of anti-arrhythmic action and is an important indicator that can be taken in judging the effectiveness in clinical arrhythmia. Conventional anti-arrhythmic agents having the prolongation effect on the refractory period as the main mechanism (such as d-sotalol belonging to Class III of the antiarrhythmic agent classification according to Vaughan

Williams) have been the therapeutic problems in inducing highly dangerous arrhythmia leading to the sudden death from such as *torsades de pointes* among others due to prolongation of action potential in ventricular muscle correlated to the prolongation effect on the refractory period, and thus becoming the therapeutic problem in arrhythmia mainly of atrial muscle (such as supraventricular tachycardia, atrial flutter, atrial fibrillation and the like).

In order to solve the problems, the inventors of the present invention carried out the investigation of compounds having the prolongation effect on the refractory period selective for atrium muscle than for ventricular muscle, and found that the compound of formula (I) or (II) has a prolongation effect on the refractory period selective for atrium muscle without any influence on the refractory period and action potential in ventricular muscle. The difference between the findings by the inventors and the prior art is in providing the prolongation effect on the refractory period selective for atrium muscle to these compound group, which may be shown by the facts that there is no influence on the action potential duration period of isolated ventricular muscle and there is no influence on QT in the electrocardiogram of anesthetized animal. From above, the compounds of the present invention show no inducing action of arrhythmia in ventricular muscle, thus they can contribute to much safer use in arrhythmia mainly of atrial muscle in comparison with the prior art. The present technical knowledge is beneficial for therapeutic or preventive uses as anti-atrial fibrillation agents, anti-atrial flutter agents and anti-atrial tachycardia agents relating to paroxysmal, chronic, preoperative, intraoperative or postoperative atrial arrhythmia, prevention in the progression leading to embolus due to arrhythmia of artial nature, prevention in the progression leading to ventricular arrhythmia or tachycardia from atrial arrhythmia or tachycardia, and averting the life threatening prognosis due to preventive action on atrial arrhythmia or tachycardia leading to ventricular arrhythmia or tachycardia.

The present invention provides a pharmaceutical composition or a veterinary pharmaceutical composition containing a compound of formula (I) or (II) in an effective amount for these treatments.

As forms of administration for the compound according to the present invention, parenteral administration forms such as injections (subcutaneous, intravenous, intramuscular and intraperitoneal injections), ointments, suppositories, aerosols and the like, and oral administration forms such as tablets, capsules, granules, pills, syrups, solutions, emulsions, suspensions and the like can be

mentioned.

The pharmaceutical or veterinary pharmaceutical composition described above contains the compound according to the present invention in an amount of about 0.01-99.5%, preferably about 0.1-30%, based on the total weight of the composition.

In addition to the compound according to the present invention or the composition containing the compound, other pharmaceutically or veterinary pharmaceutically active compounds may be contained.

Further, these compositions may contain the plurality of compounds according to the present invention.

An amount of the compound according to the present invention to be used in clinical administration may vary depending on age, weight and sensitivity of the patient, symptomatic condition and the like, but an effective amount in clinical administration is generally about 0.003-1.5 g, preferably 0.01-0.6 g, per day for adult. If necessary, however, the amount outside of the aforementioned range may be used.

The compound according to the present invention is formulated for administration by conventional pharmaceutical means.

That is, tablets, capsules, granules and pills for oral administration are prepared by using excipients such as sucrose, lactose, glucose, starch and mannitol; binders such as hydroxypropyl cellulose, syrup, gum arabic, gelatin, sorbitol, tragacanth, methyl cellulose and polyvinyl pyrrolidone; disintegrators such as starch, carboxymethyl cellulose or its calcium salt, microcrystalline cellulose and polyethylene glycol; lubricants such as talc, magnesium or calcium stearate, and silica; lubricaing agents such as sodium laurate and glycerol and the like.

Injections, solutions, emulsions, suspensions, syrups and aerosols are prepared by using solvents for the active components such as water, ethyl alcohol, isopropyl alcohol, propylene glycol, 1,3-butylene glycol and polyethylene glycol; surfactants such as sorbitan fatty acid ester, polyoxyethylene sorbitan fatty acid ester, polyoxyethylene fatty acid ester, polyoxyethylene ether of hydrogenated castor oil and lecithin; suspending agents such as carboxymethyl sodium salt, cellulose derivatives such as methyl cellulose or the like, and natural rubbers such as gum arabic, tragacanth or the like; and preserves such as p-hydroxybenzoic acid esters, benzalkonium chloride, sorbic acid salts and the like.

For ointments that are transdermally adsorptive pharmaceutics, for example, white vaseline, liquid paraffin, higher alcohols, Macrogol ointments, hydrophilic

ointments, aqueous gel-type bases and the like are used.

Suppositories are prepared by using, for example, cocoa fats, polyethylene glycol, lanolin, fatty acid triglyceride, coconut oil, polysorbate and the like.

Examples

The present invention is illustrated in detail by the Examples as follows, but the present invention is not limited to these Examples.

[Synthesis Examples]

Furthermore, Ph,Ph salen manganese complex (XX) and Cyc,Ph salen manganese complex (XY) mean optically active compounds of formula below which were synthesized according to the method similar to one described in Japanese Patent Laid-open No. Hei 7-285983.

Synthesis Example 1

(±)-trans-2,2,9-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol 3/2 maleate

2,2,9-Trimethyl-2H-pyrano[2,3-g]quinoline

To a solution of 6-amino-2,2-dimethylchromene (10.1 g, 57.7 mmol) in ethanol (500 mL), methylvinylketone (33.0 mL, 404 mmol), *m*-nitrobenzenesulfonic acid (21.1 g, 104 mmol), zinc chloride (1.97 g, 14.4 mol) and 35% hydrochloric acid (24 mL, 289

mmol) were added at room temperature and the resulting mixture was stirred at 110°C for 5 hours. Upon the completion of the reaction, ethanol was distilled off, water was added, and the resulting solution was neutralized with sodium hydrogencarbonate and extracted with ethyl acetate. The resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 38%).

Brown amorphous product

¹H-NMR(CDCl₃) δ; 1.51(s, 6H), 2.59(d, J = 0.6 Hz, 3H), 5.90(d, J = 9.9 Hz, 1H), 6,59(d, J = 9.9 Hz, 1H), 7.11(d, J = 3.6 Hz, 1H), 7.25(s, 1H), 7.68(s, 1H), 8.57(d, J = 4.4 Hz, 1H)

MS(ESI⁺)m/z; 226 [M+1]⁺

(±)-trans-2,2,9-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol

To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline (530 mg, 2.35 mmol) in dimethylsulfoxide (8 mL), *N*-bromosuccinimide (920 mg, 5.17 mmol) and water (1.6 mL) were added at room temperature and the resulting mixture was stirred at room temperature for 3 hours. Upon the completion of the reaction, water was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. Aqueous sodium hydrogencarbonate solution was added to the aqueous phase and the resulting solution was further extracted with ethyl acetate. The combined organic phases were was dried over anhydrous magnesium sulfate and the solvent was distilled off to obtain a crude product of

(±)-trans-3-bromo-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-ol. At room temperature, 1,4-dioxane (30 mL) and 1 mol/L aqueous sodium hydroxide solution (5.64 mL) were added thereto, and the resulting solution was stirred at room temperature for 2.5 hours. Upon the completion of the reaction, water was added to the reaction solution, and the resulting solution was extracted with ethyl acetate, dried over anhydrous magnesium sulfate and the solvent was distilled off to obtain a crude

product of 3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline. To the residue, 1,4-dioxane (3.2 mL), lithium perchlorate (250 mg, 2.35 mmol) and 2-phenylethylamine (0.35 mL, 2.82 mmol) were added at room temperature, and the resulting mixture was stirred at 75°C for 5 hours. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the resulting solution was extracted with ethyl acetate, the organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/1) and the aimed product was obtained (3-steps, yield: 26%).

¹H-NMR(CDCl₃) δ; 1.26(s, 3H), 1.55(s, 3H), 2.59(s, 3H), 2.83(t, J = 6.8 Hz, 2H), 2.96-3.12(m, 3H), 3.60(d, J = 10.5 Hz, 1H), 3.88(dd, J = 1.1 Hz, 10.5 Hz, 1H), 7.13(d, J = 4.2 Hz, 1H), 7.18-7.32(m, 6H), 7.98(d, J = 1.1 Hz, 1H), 8.60(d, J = 4.4 Hz, 1H) MS(ESI⁺)m/z: 363 IM+11⁺

To a solution of

(±)-trans-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol (219 mg, 0.60 mmol) in ethyl acetate (3 mL), a solution of maleic acid (77 mg, 0.66 mmol) in ethyl acetate (1 mL) was added dropwise, the resulting reaction solution was cooled to 0°C, hexane (10 mL) was added thereto, and precipitated solid was filtered off to obtain

(±)-trans-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol 3/2 maleate (yield: 72%).

Yellow crystals

mp;172-174°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 1.17(s, 3H), 1.50(s, 3H), 2.59(s, 3H), 2.94-3.37(m, 4H), 4.10(dd, J = 6.1 Hz, 9.4 Hz, 1H), 4.72(d, J = 9.4 Hz, 1H), 6.09(s, 3H), 6.33(d, J = 6.1 Hz, 1H), 7.23-7.35(m, 6H), 7.42(s, 1H), 8.43(s, 1H), 8.66(d, J = 4.1 Hz, 1H)

Synthesis Example 2

(±)-trans-2,2,7,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]qu inolin-3-ol

This compound was synthesized according to the process of Synthesis Example 1.

2,2,7,9-Tetramethyl-2H-pyrano[2,3-g]quinoline

(Yield: 59%)

Black brown oily product

¹H-NMR(CDCl₃) δ: 1.49(s, 6H), 2.54(s, 3H), 2.62(s, 3H), 5.86(d, J = 9.9 Hz, 1H), 6,55(d, J = 9.9 Hz, 1H), 7.00(s, 1H), 7.20(s, 1H), 7.60(s, 1H) MS(ESI⁺)m/z; 240[M+1]⁺

(±)-trans-3-Bromo-2,2,7,9-tetramethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-ol

(Yield: 82%)

¹H-NMR(CDCl₃) δ; 1.47(s, 3H), 1.68(s, 3H), 2.58(s, 3H), 2.70(s, 3H), 4.28(d, J = 9.6 Hz, 1H), 5.14(d, J = 9.6 Hz, 1H), 7.08(s, 1H), 7.28(s, 1H), 8.37(s, 1H) MS(ESI⁺)m/z; 336, 338 [M+1]⁺

(±)-*trans*-2,2,7,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]qu inolin-3-ol (yield: 17%)

White crystals

mp;144-147°C

¹H-NMR(CDCl₃) δ; 1.25(s, 3H), 1.54(s, 3H), 1.90(br s, 1H), 2.55(s, 3H), 2.65(s, 3H), 2.81(t, J = 6.8 Hz, 2H), 2.97-3.10(m, 2H), 3.19(br s, 1H), 3.58(d, J = 10.5 Hz, 1H), 3.85(d, J = 10.5 Hz, 1H), 7.04(s, 1H), 7.17-7.31(m, 6H), 7.91(s, 1H) MS(ESI⁺)m/z; 377 [M+1]⁺

MS(ESI⁻)m/z; 421 [M+45]⁺ (HCOOH adduct)

Synthesis Example 3

(±)-trans-2,2,8,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]qu inolin-3-ol 1 maleate

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ &$$

This compound was synthesized according to the process of Synthesis Example 1.

2,2,8,9-Tetramethyl-2H-pyrano[2,3-g]quinoline

(Yield: 50%)

¹H-NMR(CDCl₃) δ; 1.50(s, 6H), 2.50(s, 3H), 2.66(s, 3H), 5.87(d, J = 9.9 Hz, 1H), 6,57(d, J = 9.9 Hz, 1H), 7.26(s, 1H), 7.63(s, 1H), 8.48(s, 1H) MS(ESI⁺)m/z; 240 [M+1]⁺

 (\pm) -trans-3-Bromo-2,2,7,9-tetramethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-ol

(Yield: 65%)

¹H-NMR(CDCl₃) δ; 1.48(s, 3H), 1.69(s, 3H), 1.80(br s, 1H), 2.46(s, 3H), 2.56(s, 3H), 4.28(d, J = 9.6 Hz, 1H), 5.15(d, J = 9.6 Hz, 1H), 7.25(s, 1H), 8.42(s, 1H), 8.57(s, 1H) MS(ESI*)m/z; 336, 338 [M+1]*

(±)-*trans*-2,2,8,9-Tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]qu inolin-3-ol 1 maleate

(Yield: 4%)
White crystals

mp;199-203°C

¹H-NMR(DMSO-d₆) δ; 1.17(s, 3H), 1.50(s, 3H), 2.41(s, 3H), 2.49(s, 3H), 2.89-3.40(m, 4H), 4.07(dd, J = 5.5 Hz, 9.4 Hz, 1H), 4.66(d, J = 9.4 Hz, 1H), 6.05(s, 2H), 6.28(d, J = 5.5 Hz, 1H), 7.22-7.35(m, 5H), 7.43(s, 1H), 8.36(s, 1H), 8.59(s, 1H)

MS(ESI⁺)m/z; 377 [M+1] +

MS(ESI)m/z; 421 [M+45] + (HCOOH adduct)

Synthesis Example 4

(±)-trans-2,2,7-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol 3/2 maleate

$$Ph$$
 OH
 CO_2H
 CO_2H

2,2,7-Trimethyl-2*H*-pyrano[2,3-g]quinoline

To 6-amino-2,2-dimethylchromene (1.00 g, 5.71 mmol), 35% hydrochloric acid (1.43 mL, 17.1 mmol), p-chloranil (1.40 g, 5.71 mmol) and n-butanol (1.3 mL) were added at room temperature and the temperature was increased to 120° C. A solution of crotyl aldehyde (0.567 mL, 6.84 mmol) in n-butanol (0.52 mL) was added and the resulting mixture was stirred at 120° C for 20 minutes. A solution of zinc chloride (0.777 g, 5.71 mmol) in tetrahydrofuran (10 mL) was added, and the resulting mixture was stirred at 120° C for 20 minutes. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added, and the resulting solution was extracted with ethyl acetate and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 2/1), and recrystallized from ethyl acetate to obtain the aimed product (yield: 22%).

Gray solid

¹H-NMR(CDCl₃) δ; 1.48(s, 6H), 2.67(s, 3H), 5.87(d, J = 9.9 Hz, 1H), 6,55(d, J = 9.9 Hz, 1H), 7.05(s, 1H), 7.16(d, J = 8.5 Hz, 1H), 7.64(s, 1H), 7.86(d, J = 8.5 Hz, 1H) MS(ESI⁺)m/z; 226 [M+1] ⁺

MS(ESI)m/z; 225 [M] +

(±)-trans-3-Bromo-2,2,7-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-ol

This compound was synthesized according to the process of Synthesis Example 1.

(Yield: 24%)

(±)-trans-2,2,7-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol 3/2 maleate

(Yield: 12%)

White crystals

¹H-NMR(DMSO-d₆) δ; 1.15(s, 3H), 1.48(s, 3H), 2.63(s, 3H), 2.70-3.38(m, 4H), 4.09(dd, J = 5.8 Hz, 9.4 Hz, 1H), 4.68(d, J = 9.4 Hz, 1H), 6.08(s, 3H), 6.29(d, J = 5.8 Hz, 1H), 7.22-7.35(m, 6H), 7.40(s, 1H), 8.10(d, J = 8.5 Hz, 1H), 8.33(s, 1H)

MS(ESI*)m/z; 363 [M+1] +

MS(ESI)m/z; 407 [M+45] + (HCOOH adduct)

Synthesis Example 5

(±)-trans-2,2,8-Trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol 2 maleate

$$Ph$$
 OH
 CO_2H
 CO_2H

This compound was synthesized according to the process of Synthesis Example 4.

2,2,8-Trimethyl-2H-pyrano[2,3-g]quinoline

(Yield: 17%)

¹H-NMR(CDCl₃) δ; 1.48(s, 6H), 2.45(s, 3H), 5.87(d, J = 9.9 Hz, 1H), 6.56(d, J = 9.9 Hz, 1H), 7.00(s, 1H), 7.64(s, 1H), 7.70(s, 1H), 8.54(d, J = 8.5 Hz, 1H) MS(ESI⁺)m/z; 226 [M+1]⁺

(±)-trans-3-Bromo-2,2,8-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-ol

(Yield: 54%)

MS(ESI⁺)m/z; 322, 324 [M+1] ⁺

(±)-*trans*-2,2,8-Trimethyl-4-[(2-phen**y**lethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoli n-3-ol 2 maleate

(Yield: 20%)

White crystals

¹H-NMR(DMSO-d₆) δ; 1.15(s, 3H), 1.49(s, 3H), 2.45(s, 3H), 2.97-3.39(m, 4H), 4.09(dd, J = 6.1 Hz, 9.4 Hz, 1H), 4.71(d, J = 9.1 Hz, 1H), 6.15(s, 4H), 6.32(d, J = 6.3 Hz, 1H), 7.19-7.36(m, 5H), 7.97(s, 1H), 8.39(s, 1H), 8.67(s, 1H)

Synthesis Example 6

(±)-trans-7-Chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate

$$CI$$
 OH CO_2H CO_2H

To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline (1.56 g, 6.92 mmol) in chloroform (15.6 mL), a solution of *m*-chloroperbenzoic acid (2.61 g, 15.2 mmol) in chloroform (6.4 mL)-methanol (1.6 mL) was added dropwise at room temperature and the resulting mixture was stirred at room temperature for 1.5 hour. Upon the completion of the reaction, the reaction solution was extracted with aqueous sodium thiosulfate solution and the resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, chloroform

(33 mL), *p*-toluenesulfonyl chloride (1.32 g, 6.92 mmol) and potassium carbonate (0.954 g, 6.92 mmol) were added to the residue at room temperature, and the resulting mixture was stirred at 70°C for 3 hours. Upon the completion of the reaction, water was added to the reaction solution, and it was extracted with chloroform. The resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 67%).

Pale yellow solid

¹H-NMR(CDCl₃) δ; 1.42(s, 6H), 2.48(d, J = 0.8 Hz, 3H), 5.83(d, J = 9.9 Hz, 1H), 6.47(d, J = 9.9 Hz, 1H), 7.03(d, J = 3.6 Hz, 1H), 7.11(s, 1H), 7.50(s, 1H) MS(ESI⁺)m/z; 260 [M+1]⁺

(±)-trans-3-Bromo-7-chloro-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-ol

Hereinafter, the aimed compound was synthesized according to the process of Synthesis Example 1.

(Yield: 44%)

MS(ESI+)m/z; 356, 358 [M+1]+

(±)-trans-7-Chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol 1 maleate

(Yield: 58%)

White crystals

mp: 221-226°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 1.17(s, 3H), 1.49(s, 3H), 2.60(s, 3H), 2.93-3.32(m, 4H), 4.05(m, 1H), 4.65(d, J = 9.4 Hz, 1H), 6.05(s, 2H), 6.28(br s, 1H), 7.22-7.34(m, 5H), 7.43(s, 2H), 8.32(s, 1H)

MS(ESI⁺)m/z; 397 [M+1] ⁺

MS(ESI)m/z; 441 [M+45] + (HCOOH adduct)

Synthesis Example 7

(±)-trans-3-Hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2, 3-q]quinoline-7-carbonitrile 1 maleate

2,2,9-Trimethyl-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile

To a solution of 2,2,9-trimethyl-2H-pyrano[2,3-g]quinoline (4.36 g, 19.3 mmol) in chloroform (43.6 mL), a solution of *m*-chloroperbenzoic acid (7.35 g, 42.6 mmol) in chloroform (17.4 mL)-methanol (4.36 mL) was added dropwise at room temperature and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, the reaction solution was extracted with aqueous sodium thiosulfate solution and the resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetonitrile (19.3 mL), trimethylsilylcyanide (7.27 mL, 57.9 mmol) and triethylamine (5.38 mL, 38.6 mmol) were added to the residue at room temperature, and the resulting solution was stirred at 70°C for 3.5 hours. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with chloroform and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 55%). Pale vellow solid

¹H-NMR(CDCl₃) δ; 1.52(s, 6H), 2.62(d, J = 0.6 Hz, 3H), 5.97(d, J = 9.9 Hz, 1H), 6.58(d, J = 9.9 Hz, 1H), 7.23(s, 1H), 7.40(s, 1H), 7.71(s, 1H) MS(ESI⁺)m/z; 251 [M+1]⁺

(±)-trans-3-Bromo-4-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile

Hereinafter, the aimed compound was synthesized according to the process of Synthesis Example 1.

(Yield: 36%)

MS(ESI⁺)m/z; 349 [M+1] ⁺

(±)-trans-3-Hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2, 3-g]quinoline-7-carbonitrile 1 maleate

White crystals

mp: 218-220°C (decomposition)

¹H-NMR(DMSO-d₆) δ ; 1.20(s, 3H), 1.51(s, 3H), 2.65(s, 3H), 2.96-3.33(m, 4H),

4.04-4.06(m, 1H), 4.64(br s, 1H), 6.05(s, 2H), 6.29 (br s, 1H), 7.25-7.31(m, 5H),

7.50(s, 1H), 7.85(s, 1H), 8.49(s, 1H)

MS(ESI*)m/z; 388 [M+1] *

MS(ESI⁻)m/z; 432 [M+45] ⁺ (HCOOH adduct)

Synthesis Example 8

(±)-trans-3,3-Dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1 *H*-pyrano[3,2-f]quinolin-2 -ol

6-[(1,1-dimethyl-2-propynyl)oxy]quinoline

A solution of 2-methyl-3-butyn-2-ol (2.45 mL, 25.1 mmol) and 1,8-diazabicyclo-[5.4.0]-7-undecene (4.25 mL, 28.4 mmol) in acetonitrile (15.5 mL) was stirred 0°C for 30 minutes, and trifluoroacetic anhydride (3.55 mL, 25.1 mmol) was added dropwise. The resulting mixture was added dropwise to a mixed solution

of 6-hydroxyquinoline (2.43 g, 16.7 mmol), copper (I) chloride (8.3 mg, 0.0835 mmol), acetonitrile (15.5 mL) and 1,8-diazabicyclo-[5.4.0]-7-undecene (4.25 mL, 28.4 mmol) at 0°C, and stirred at 0°C for 3 hours. The resulting solution was acidified with 1 mol/L HCl and extracted with ethyl acetate, and the resulting aqueous phase was neutralized with aqueous sodium hydrogencarbonate solution, extracted with ethyl acetate, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/1 to 1/3) and the aimed product was obtained.

Pale yellow solid

mp: 65-67°C

¹H-NMR(CDCl₃) δ; 1.86(s, 6H), 2.70(s, 1H), 7.69-7.71(2H), 7.80(s, 1H), 8.33(d, J = 8.3 Hz, 1H), 8.45(d, J = 8.3 Hz 1H), 9.01(br s, 1H)

MS(GC)m/z; 211 [M] *

3,3-Dimethyl-3*H*-pyrano[3,2-f]quinoline

A solution of 6-[(1,1-dimethyl-2-propynyl)oxy]quinoline (16.7 mmol) in 1,2-dichlorobenzene (10 mL) was stirred at 180°C for 1 hour. Upon the completion of the reaction, the solvent was distilled off, and the residue was recrystallized from hexane-ethyl acetate to obtain the aimed compound (2-steps, quant.).

Green crystals

mp: 104-107°C

¹H-NMR(CDCl₃) δ; 1.54(s, 6H), 5.89(d, J = 10.2 Hz, 1H), 6.93(d, J = 10.2 Hz, 1H), 7.50(d, J = 9.1 Hz, 1H), 7.73(br s, 1H), 8.31(d, J = 9.1 Hz, 1H), 8.74(d, J = 8.5 Hz, 1H), 9.03(br s, 1H)

MS(GC)m/z; 211[M] +

(±)-trans-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinolin-2 -ol

Hereinafter, the aimed compound was synthesized according to the process of Synthesis Example 1.

mp: 180-182°C

¹H-NMR(CDCl₃) δ; 1.32(s, 3H), 1.44(s, 3H), 1.63(br s, 1H), 2.43(br s, 1H), 2.69-2.84(m, 3H), 2.92-2.97(m, 1H), 3.83(d, J = 5.0 Hz, 1H), 4.09(d, J = 5.5 Hz, 1 H), 7.10-7.29(m, 6H), 7.86(d, J = 9.1 Hz, 1H), 8.13(d, J = 7.7 Hz, 1H), 8.71(dd, J = 1.7 Hz, 4.1 Hz, 1H)

MS(ESI⁺)m/z; 349 [M+1] ⁺

MS(ESI⁻)m/z; 393 [M+45] * (HCOOH adduct)

Synthesis Example 9

(±)-trans-8-Chloro-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f] quinolin-2-ol

By use of 3,3-dimethyl-3H-pyrano[3,2-f]quinoline, the aimed compound was synthesized similarly to the process of Synthesis Example 6.

8-Chloro-3,3-dimethyl-3*H*-pyrano[3,2-f]quinoline

(Yield: 82%)

Red-brown oily product

¹H-NMR(CDCl₃) δ; 1.49(s, 6H), 5.77(d, J = 9.9 Hz, 1H), 6.87(d, J = 9.9 Hz, 1H), 7.27(d, J = 9.1 Hz, 1H), 7.34(d, J = 8.8 Hz, 1H), 7.80(d, J = 9.1 Hz, 1H), 8.19(d, J = 8.8 Hz, 1H)

MS(ESI⁺)m/z; 246 [M+1] ⁺

(±)-trans-2-Bromo-8-chloro-3,3-dimethyl-2,3-dihydro-1H-pyrano[3,2-f]quinolin-1-ol

(Yield: 45%)

 (\pm) -trans-8-Chloro-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1H-pyrano[3,2-f] quinolin-2-ol

(Yield: 60%)

White crystals

mp: 141-143°C

¹H-NMR(CDCl₃) δ; 1.28(s, 3H), 1.44(s, 3H), 1.64(br s, 2H), 2.65-2.78(m, 3H), 2.86-2.96(m, 1H), 3.84(d, J = 6.1 Hz, 1H), 4.06(d, J = 5.8 Hz, 1H), 7.08-7.30(m, 7H**)**,

7.98(d, J = 9.1 Hz, 1H), 8.22(d, J = 8.8 Hz, 1H)

MS(ESI*)m/z; 383 [M+1] *

MS(ESI⁻)m/z; 427 [M+45] + (HCOOH adduct)

Synthesis Example 10

(±)-trans-2-Hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinoline-8-carbonitrile

By use of 3,3-dimethyl-3*H*-pyrano[3,2-f]quinoline, the aimed compound was synthesized similarly to the process of Synthesis Example 7.

3,3-Dimethyl-3H-pyrano[3,2-f]quinoline-8-carbonitrile

(Yield: quant.)

Yellow solid

¹H-NMR(CDCl₃) δ; 1.52(s, 6H), 5.80(d, J = 9.9 Hz, 1H), 6.89(d, J = 10.2 Hz, 1H), 7.37(d, J = 9.4 Hz, 1H), 7.65(d, J = 8.8 Hz, 1H), 7.95(d, J = 9.4 Hz, 1H), 8.64(d, J = 8.8 Hz, 1H)

MS(ESI*)m/z; 237 [M+1] *

MS(ESI⁻)m/z; 235 [M-1] +

(±)-trans-2-Bromo-1-hydroxy-3,3-dimethyl-2,3-dihydro-1*H*-pyrano[3,2-f]quinoline-8-car bonitrile

(Yield: 49%)

¹H-NMR(CDCl₃) δ; 1.50(s, 3H), 1.69(s, 3H), 2.72(d, J = 4.1 Hz, 1H), 4.35(d, J = 7.2 Hz, 1H), 5.43(dd, J = 3.9 Hz, 7.2 Hz, 1H), 7.36(d, J = 9.1 Hz, 1H), 7.70(d, J = 8.8 Hz, 1H), 8.03(d, J = 9.4 Hz, 1H), 8.72(d, J = 8.5 Hz, 1H)

MS(ESI⁺)m/z; 333, 335 [M+1] ⁺

MS(ESI)m/z; 379 [M+45] + (HCOOH adduct)

(±)-trans-2-Hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1*H*-pyrano[3,2-f]quinoline-8-carbonitrile

(Yield: 72%)
White crystals

---- 02 06ºC

mp: 93-96°C

¹H-NMR(CDCl₃) δ; 1.30(s, 3H), 1.46(s, 3H), 1.60(br s, 3H), 2.13(br s, 1H), 2.66-2.79(m, 3H), 2.88-2.98(m, 1H), 3.87(d, J = 5.8 Hz, 1H), 4.08(d, J = 6.1 Hz, 1H), 7.09(d, J = 6.3 Hz, 1H), 7.10(d, J = 7.4 Hz, 1H), 7.23-7.27(m, 3H), 7.30(d, J = 9.1 Hz, 1H), 7.41(d, J = 8.8 Hz, 1H), 7.92(d, J = 9.1 Hz, 1H), 8.38(d, J = 8.5 Hz, 1H) MS(ESI⁺)m/z; 374 [M+1]⁺

MS(ESI)m/z; 418 [M+45] + (HCOOH adduct)

Synthesis Example 11

 (\pm) -trans-2-Hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1H-pyrano[3,2-f]quinoline-8-carboxamide

To a solution of

(±)-trans-2-hydroxy-3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1H-pyrano[3,2-f

]quinoline-8-carbonitrile (400 mg, 1.07 mmol) in *t*-butanol (40 mL), potassium hydroxide (800 mg, 14.3 mmol) was added at room temperature and the resulting mixture was stirred at 90°C for 2 hour. Upon the completion of the reaction, aqueous sodium chloride solution was added to the reaction solution, and it was extracted with ethyl acetate and the resulting organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/1) and recrystallized from hexane-ethyl acetate to obtain the aimed product (yield: 54%).

White crystals

mp: 197-199°C

¹H-NMR(CDCl₃) δ; 1.32(s, 3H), 1.47(s, 3H), 1.71(br s, 2H), 2.29(br s, 1H), 2.69-2.76(m, 3H), 2.89-2.97(m, 1H), 3.86(br s, 1H), 4.13(d, J = 5.8 Hz, 1H), 5.62(br s, 1H), 7.10(d, J = 6.9 Hz, 1H), 7.10(d, J = 7.4 Hz, 1H), 7.20-7.28(m, 4H), 7.89(d, J = 9.4 Hz, 1H), 7.98(br s, 1H), 8.07(d, J = 8.8 Hz, 1H), 8.31(d, J = 8.8 Hz, 1H)

MS(ESI⁺)m/z; 392 [M+1] ⁺

MS(ESI⁻)m/z; 436 [M+45] + (HCOOH adduct)

Synthesis Example 12

 $(3R^*,4S^*)$ -2,2,7,9-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]q uinolin-3-ol 1 maleate

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

 $(3R^*,4R^*)$ -3,4-epoxy-2,2,7,9-tetramethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoline

To a solution of 2,2,7,9-tetramethyl-2*H*-pyrano[2,3-g]quinoline (4.64 g, 19.4 mmol) in ethyl acetate (70 mL), *N*-methyl imidazole (0.303 mL, 3.88 mmol) and Ph,Ph salen manganese complex (XX) (201 mg, 0.194 mmol) were added at room temperature and aqueous sodium hypochlorite solution (25.6 g, 1.513 mol/kg, 38.8 mmol) was added dropwise, and the resulting mixture was stirred for 1 hour. Further, in water bath, aqueous sodium hypochlorite solution (25.6 g, 1.513 mol/kg, 38.8

mmol) was added, and the resulting mixture was stirred in water bath for 1 hour. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, the resulting mixture was filtered through celite and extracted. The organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/3) and the aimed product was obtained (yield: 68%).

> 99.9% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 5.7 min.

¹H-NMR(CDCl₃) δ; 1.30(s, 3H), 1.64(s, 3H), 2.56(s, 3H), 2.66(s, 3H), 3.59(d, J = 4.4 Hz, 1H), 4.14(d, J = 4.4 Hz, 1H), 7.08(s, 1H), 7.29(s, 1H), 8.04(s, 1H) MS(ESI⁺)m/z; 256 [M+1]⁺

 $(3R^*,4S^*)$ -2,2,7,9-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]q uinolin-3-ol 1 maleate

To a solution of

(3R*,4R*)-3,4-epoxy-2,2,7,9-tetramethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (0.80 g, 3.14 mmol) in 1,4-dioxane (1.6 mL), lithium perchlorate (334 mg, 3.14 mmol) and 2-phenylethylamine (0.473 mL, 3.77 mmol) were added at room temperature. and the resulting mixture was stirred at 70°C for 1 hour. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with ethyl acetate and the resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (ethyl acetate). Further, after distilling off the solvent, ethyl acetate (2 mL) was added and a solution of maleic acid (376 mg, 3.23 mmol) in ethyl acetate (8mL) was added dropwise. The resulting precipitated solid was filtered to obtain the aimed product (yield: 86%).

White crystals

mp: 215-219°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 1.16(s, 3H), 1.49(s, 3H), 2.55(s, 3H), 2.58(s, 3H), 2.93-3.39 (m, 4H), 4.07(dd, J = 6.4 Hz, 9.4 Hz, 1H), 4.64(d, J = 9.4 Hz, 1H), 6.05(s, 2H), 6.27(d, J = 5.8 Hz, 1H), 7.24-7.26(m, 4H), 7.30(s, 1H), 7.33(s, 1H), 7.36(s, 1H), 8.31(s, 1H) MS(ESI⁺)m/z; 377 [M+1]⁺

MS(ESI⁻)m/z; 421 [M+45] + (HCOOH adduct)

Synthesis Example 13

 $(3R^*,4S^*)$ -2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoli n-3-ol 1 maleate

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

This compound was synthesized according to the process of Synthesis Example 12.

 $(3R^*,4R^*)$ -3,4-epoxy-2,2,7-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoline

99.3% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 6.2 min.

¹H-NMR(CDCl₃) δ; 1.28(s, 3H), 1.64(s, 3H), 2.71(s, 3H), 3.59(d, J = 4.4 Hz, 1H), 4.15(d, J = 4.4 Hz, 1H), 7.13(s, 1H), 7.23(d, J = 8.5 Hz, 1H), 7.91(d, J = 8.5 Hz, 1H), 8.05(s, 1H)

MS(ESI*)m/z; 242 [M+1]*

 $(3R^*,4S^*)$ -2,2,7-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoli n-3-ol 1 maleate

White crystals

mp: 214-217°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 1.15(s, 3H), 1.48(s, 3H), 2.62(s, 3H), 2.93-3.14 (m, 4H), 4.03-4.07(m, 1H), 4.61(br s, 1H), 6.04(s, 2H), 6.23(br s, 1H), 7.23-7.39(m, 7H), 8.09(d, J = 8.5 Hz, 1H), 8.31(s, 1H)

MS(ESI*)m/z; 363 [M+1] *

MS(ESI⁻)m/z; 407 [M+45] ⁺ (HCOOH adduct)

Synthesis Example 14

(3R*,4S*)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2

,3-g]quinoline-7-carbonitrile 1 maleate

This compound was synthesized according to the process of Synthesis Example 12.

 $(3R^*,4R^*)$ -3,4-epoxy-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoline-7-carbonitrile

(Yield: 33%)

99.1% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 18.6 min.

¹H-NMR(CDCl₃) δ; 1.33(s, 3H), 1.66(s, 3H), 2.65(s, 3H), 3.64(d, J = 4.1 Hz, 1H), 4.17(d, J = 4.4 Hz, 1H), 7.33(s, 1H), 7.47(s, 1H), 8.18(s, 1H)

MS(ESI⁺)m/z; 267 [M+1]⁺ MS(ESI⁻)m/z; 265 [M-1]⁺

 $(3R^*,4S^*)$ -3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoline-7-carbonitrile 1 maleate

(Yield: 23%)

Pale brown crystals

 1 H-NMR(DMSO-d₆) δ; 1.20(s, 3H), 1.52(s, 3H), 2.66(s, 3H), 2.98-3.33(m, 4H), 4.09(m, 1H), 4.71(br s, 1H), 6.09(s, 2H), 6.33(br s, 1H), 7.23-7.34(m, 5H), 7.51(s, 1H), 7.86(s, 1H), 8.51(s, 1H)

MS(ESI*)m/z; 388 [M+1]*

MS(ESI⁻)m/z; 432 [M+45] + (HCOOH adduct)

Synthesis Example 15

 $(3R^*,4S^*)$ -3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoline-7-carboxamide

$$H_2N$$
 O
 $H_{\underline{\underline{N}}}$
 OH
 OH

This compound was synthesized from

 $(3R^*,4S^*)$ -3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoline-7-carbonitrile similarly to the process of Synthesis Example 11 (yield: 9%).

White crystals

mp: 168-169°C

¹H-NMR(CDCl₃) δ ; 1.26(s, 3H), 1.57(s, 3H), 1.83(br s, 3H), 2.65(s, 2H), 2.90-3.16(m, 4H), 3.66(d, J = 10.2 Hz, 1H), 3.95(d, J = 10.5 Hz, 1H), 5.61(br s, 1H), 7.24-7.36(m, 5H), 7.85(s, 1H), 8.00(br s, 1H), 8.04(s, 1H)

MS(ESI⁺)m/z; 406 [M+1] +

MS(ESI⁻)m/z; 450 [M+45] + (HCOOH adduct)

Synthesis Example 16

 $(3R^*,4S^*)$ -{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-q]quinolin-7-yl}ethanone 1 maleate

This compound was synthesized according to the process of Synthesis Example 12.

 $(3R^*,4S^*)$ -{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-7-yl}ethanone

To a solution of

(3R*,4S*)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile (120 mg, 0.309 mmol) in benzene (1.6 mL)-diethyl ether

(1.4 mL), a solution of 3.0 M methyl magnesium bromide in diethyl ether (0.30 mL) was added dropwise at 0-5°C, and the resulting mixture was stirred for 2 hours. A solution of 3.0 M methyl magnesium bromide in diethyl ether (0.50 mL) was added dropwise at 0-5°C, and the resulting mixture was further stirred for 30 minutes. Upon the completion of the reaction, aqueous ammonium chloride solution was added and the resulting solution was extracted with ethyl acetate. The resulting organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography and the aimed product was obtained (yield: 25%).

¹H-NMR(CDCl₃) δ; 1.19(s, 3H), 1.49(s, 3H), 2.53(d, J = 0.8 Hz, 3H), 2.76(s, 3H), 2.77-3.06(m, 5H), 3.55(d, J = 10.5 Hz, 1H), 3.81(dd, J = 1.4 Hz, 10.5 Hz, 1H), 7.15-7.29(m, 6H), 7.78(s, 1H), 7.85(d, J = 1.4 Hz, 1H) MS(ESI⁺)m/z; 405 [M+1] ⁺

 $(3R^*,4S^*)$ -{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-yl}ethanone 1 maleate

To a solution of

(3R*,4S*)-{3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-yl}ethanone (31.3 mg, 0.077 mmol) in ethyl acetate (2 mL), a solution of maleic acid (10.0 mg, 0.086 mmol) in ethyl acetate (2 mL) was added dropwise, and precipitated solid was filtered to obtain the aimed product (yield: 80%). White crystals

mp: 230-234°C (decomposition)

 1 H-NMR(DMSO-d₆) δ; 1.18(s, 3H), 1.51(s, 3H), 2.66(s, 3H), 2.74(s, 3H),2.98-3.34(m, 4H), 4.10(m, 1H), 4.66(br s, 1H), 6.05(s, 2H), 6.29(br s, 1H), 7.25-7.36(m, 5H), 7.48(s, 1H), 7.87(s, 1H), 8.56(s, 1H)

Synthesis Example 17

 $(1S^*, 2R^*)$ -3,3-dimethyl-1-[(2-phenylethyl)amino]-2,3-dihydro-1H-pyrano[3,2-f]quinolin-2-ol

This compound was synthesized according to the process of Synthesis

Example 12.

(Yield: 2-steps, 4%)

White crystals

mp: 170-171°C

¹H-NMR(CDCl₃) δ; 1.31(s, 3H), 1.45(s, 3H), 1.61(br s, 6H), 2.71-2.84(m, 3H), 2.91-2.97(m, 1H), 3.83(d, J = 5.5 Hz, 1H), 4.11(d, J = 5.5 Hz, 1H), 7.12(d, J = 7.98 Hz, 1H), 7.18-7.25(m, 5H), 7.90(d, J = 9.1 Hz, 1H), 8.15(d, J = 8.5 Hz, 1H), 8.73(dd, J = 1.4 Hz, 4.1 Hz, 1H)

MS(ESI⁺)m/z; 349 [M+1] +

MS(ESI)m/z; 393 [M+45] + (HCOOH adduct)

Epoxy form, 97.1% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 7.0 min.

Synthesis Example 18

(3R*,4S*)-7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-py rano[2,3-g]quinolin-3-ol 1 maleate

$$\begin{array}{c|c} H \underline{\underline{N}} & Ph \\ \hline \\ O & OH \\ \hline \\ CO_2 H \end{array}$$

This compound was synthesized according to the process of Synthesis Example 12.

(2,2,9-trimethyl-2H-pyrano[2,3-g]quinolin-7-yl)-methyl acetate

To a solution of 2,2,7,9-tetramethyl-2*H*-pyrano[2,3-g]quinoline (3.0 g, 12.5 mmol) in chloroform (30.0 mL), a solution of *m*-chloroperbenzoic acid (4.76 g, 27.6 mmol) in chloroform (12 mL)-methanol (3 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 30 minutes. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, and it was extracted. The resulting organic phase was washed with sodium hydrogencarbonate and then with aqueous sodium chloride

solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetic anhydride (12 mL) was added to the residue, and the resulting mixture was stirred at 150°C for 1 hour. Upon the completion of the reaction, acetic anhydride was distilled off, the residue was neutralized with aqueous sodium carbonate solution, extracted with chloroform, and the resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 64%).

Black oily product

¹H-NMR(CDCI₃) δ; 1.50(s, 6H), 2.17(s, 3H), 2.61(s, 3H), 5.30(s, 2H), 5.90(d, J = 9.91 Hz, 1H), 6.57(d, J = 9.9 Hz, 1H), 7.19(s, 1H), 7.24(s, 1H), 7.70(s, 1H) MS(ESI⁺)m/z; 298 [M+1] ⁺

 $(3R^*,4R^*)$ -(3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-7-yl)-methylacetate

> 99.9% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 5.4 min. MS(ESI⁺)m/z; 314 [M+1]⁺

 $(3R^*,4S^*)$ -7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-py rano[2,3-g]quinolin-3-ol

To a solution of

 $(3R^*,4R^*)$ -(3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-7-yl)-methyl acetate (403 mg, 1.29 mmol) in 1,4-dioxane (1 mL), lithium perchlorate (137 mg, 1.29 mmol) and 2-phenylethylamine (0.195 mL, 1.55 mmol) were added at room temperature and the resulting mixture was stirred at 70°C for 1.5 hour. Upon the

completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with ethyl acetate. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 32%).

¹H-NMR(CDCl₃) δ; 1.24(s, 3H), 1.55(s, 3H), 2.58(s, 3H), 2.87-3.08(m, 5H), 3.63(d, J = 10.2 Hz, 1H), 3.81(d, J = 10.5 Hz, 1H), 4.82(s, 2H), 7.02(s, 1H), 7.23-7.36(m, 6H), 7.75(s, 1H)

MS(ESI⁺)m/z; 393 [M+1] +

MS(ESI⁻)m/z; 437 [M+45] ⁺ (HCOOH adduct)

(3R*,4S*)-7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-py rano[2,3-g]quinolin-3-ol 1 maleate

To a solution of

 $(3R^*,4S^*)$ -7-hydroxymethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-py rano[2,3-g]quinolin-3-ol (157 mg, 0.407 mmol) in ethyl acetate (4 mL), a solution of maleic acid (52 mg, 0.448 mmol) in ethyl acetate (2mL) was added dropwise, and precipitated solid was filtered to obtain the aimed compound (yield: 80%).

Pale yellow crystals

mp: 216-221°C

¹H-NMR(DMSO-d₆) δ; 1.17(s, 3H), 1.50(s, 3H), 2.60(s, 3H), 2.98-3.40(m, 4H), 4.06-4.11(m, 1H), 3.81(d, J = 10.5 Hz, 1H), 4.66-4.69(3H), 5.50(br s, 1H), 6.06(s, 2H), 6.30(br s, 1H), 7.23-7.35(m, 5H), 7.40(s, 1H), 7.47(s, 1H), 8.35(s, 1H)

Synthesis Example 19

(3R*,4S*)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3 -g]quinolin-3-ol 1 maleate

This compound was synthesized according to the process of Synthesis Example 12.

 $(3R^*, 4R^*)$ -7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoline

(Yield: 78%)

97.1% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 18.9 min.

Yellow amorphous product

¹H-NMR(CDCl₃) δ; 1.28(s, 3H), 1.65(s, 3H), 2.59(d, J = 0.8 Hz, 3H), 3.60(d, J = 4.4 Hz, 1H), 4.13(d, J = 4.4 Hz, 1H), 7.19(s, 1H), 7.29(d, 1H), 8.02(s, 1H) MS(\mathbb{E} SI⁺)m/z; 276 [M+1] ⁺

 $(3R^*, 4S^*)$ -7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3 -g]quinolin-3-ol 1 maleate (2-steps, yield: 34%)

Synthesis Examples 20-49

Synthesis Examples 20-49 were carried out similarly to the process of Synthesis Example 19.

 HN^{-R}

Synthesis Example 20

 $(3R^*,4S^*)$ -4-(benzylamino)-7-chloro-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quino lin-3-ol

(Yield: 81%)

Colorless amorphous product

 $^{1}\text{H-NMR}$ (CDCI₃) δ : 1.28 (s, 3H), 1.58 (s, 3H), 1.60 (br s, 1H), 2.60 (s, 3H), 3.12 (s,

1H), 3.72 (d, J = 10.3 Hz, 1H), 3.91 (d, J = 10.3 Hz, 1H), 3.85-4.00 (m, 2H), 7.17 (s, 1H), 7.30-7.40 (m, 6H), 8.08 (s, 1H).

MS (ESI⁺) m / z; 383 [M+1]⁺

MS (ESI) m / z; $427[M+45]^{\dagger}$ (HCOOH adduct)

Synthesis Example 21

 $(3R^*,4S^*)$ -4-{[((1,3-benzodioxol-5-yl)methyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 92%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.57 (s, 3H), 2.59 (s, 3H), 3.70 (d, J = 10.3 Hz, 1H), 3.82 (ABq, J = 12.8 Hz, 2H), 3.97 (dd, J = 10.3, 1.2 Hz, 1H), 5.96 (s, 2H), 6.77 (d, J = 8.0 Hz, 1H), 6.82 (dd, J = 8.0, 1.6 Hz, 1H), 6.89 (d, J = 1.6 Hz, 1H), 7.13 (s, 1H), 7.30 (s, 1H), 8.04 (s, 1H)

MS (ESI⁺) m / z; 427 [M+1]⁺

Synthesis Example 22

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-[(3-phenylpropyl)amino]-3,4-dihydro-2H-pyrano[2, 3-g]quinolin-3-ol

(Yield: 72%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.57 (s, 3H), 1.80-1.95 (m, 2H), 2.59 (s, 3H), 2.65-2.85 (m, 5H), 3.24 (s, 1H), 3.61 (d, J = 10.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 7.10-7.20 (m, 3H), 7.25-7.35 (m, 3H), 7.94 (s, 1H).

MS (ESI⁺) m / z; 411 [M+1]⁺

MS (ESI⁻) m / z; 455 [M+45]⁺ (HCOOH adduct)

Synthesis Example 23

 $(3R^*,4S^*)$ -7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 96%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.25 (s, 3H), 1.55 (s, 3H), 1.57 (br s, 1H), 2.58 (s, 3H), 2.80 (t, J = 6.9 Hz, 2H), 2.90-3.10 (m, 3H), 3.58 (d, J = 10.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 6.95-7.05 (m, 2H), 7.15-7.20 (m, 3H), 7.26 (s, 1H), 7.89 (s, 1H).

MS (ESI⁺) m / z; 415 [M+1]⁺

Synthesis Example 24

 $(3R^*,4S^*)$ -7-chloro-4-{[2-(2-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 79%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.25 (s, 3H), 1.54 (s, 3H), 1.61 (br s, 1H), 2.57 (s, 3H), 2.86 (t, J = 6.9 Hz, 2H), 2.95-3.10 (m, 3H), 3.56 (d, J = 10.4 Hz, 1H), 3.85 (d, J = 10.4 Hz, 1H), 7.00-7.25 (m, 6H), 7.90 (s, 1H).

MS (ESI⁺) m / z; 415 [M+1]⁺

Synthesis Example 25

 $(3R^*,4S^*)$ -7-chloro-4-{[2-(4-chlorophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 78%)

Colorless amorphous product

Synthesis Example 26

 $(3R^*,4S^*)$ -4-{[2-(4-aminophenyl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2, 3-g]quinolin-3-ol

(Yield: 40%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.23 (s, 3H), 1.55 (s, 3H), 1.58 (br s, 3H), 2.57 (s, 3H), 2.71 (t, J = 7.4 Hz, 2H), 2.85-3.05 (m, 2H), 3.11 (br s, 1H), 3.57 (d, J = 10.4 Hz, 1H), 3.84 (d, J = 10.4 Hz, 1H), 6.65 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H), 7.11 (s, 1H), 7.25 (s, 1H), 7.81 (s, 1H).

MS (ESI⁺) m / z; 412 [M+1]⁺

MS (ESI⁻) m / z; 456 [M+45]⁺ (HCOOH adduct)

Synthesis Example 27

 $(3R^*,4S^*)$ -7-chloro-4-[(2-hydroxy-2-phenylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 72%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.27 (s, 1.5H), 1.28 (s, 1.5H), 1.56 (s, 3H), 1.77(br s, 2H), 2.57 (s, 3H), 2.85-3.15 (m, 2H), 3.68 (d, J = 10.2 Hz, 1H), 3.75 (d, J = 10.2 Hz, 1H), 4.75-4.85 (m, 1H), 7.25 (s, 1H), 7.27-7.40 (s, 6H), 7.99 (s, 0.5H), 8.00 (s, 0.5H). MS (ESI⁺) m / z; 413[M+1]⁺ MS (ESI⁻) m / z; 457[M+45]⁺ (HCOOH adduct)

Synthesis Example 28

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-[(2-phenylbutyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 50%)

Pale brown amorphous product

¹H-NMR (CDCl₃) δ: 0.86 (t, J = 7.3 Hz, 3H), 1.20 (s, 3H), 1.53 (s, 3H), 1.51-1.71 (m, 2H), 2.57 (s, 3H), 2.57-2.64 (m, 1H), 2.86 (dd, J = 11.6, 9.1 Hz, 1H), 2.86 (dd, J = 11.6, 5.2 Hz, 1H), 3.55 (d, J = 10.2 Hz, 1H), 3.74 (d, J = 10.2 Hz, 1H), 7.15 (s, 1H), 7.20-7.32 (m, 4H), 7.35-7.41 (m, 2H), 7.74 (s, 1H)

Synthesis Example 29

 $(3R^*,4S^*)$ -4-{[2-(1,3-benzodioxol-5-yl)ethyl]amino}-7-chloro-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 62%)

Pale brown amorphous product

¹H-NMR (CDCl₃) δ: 1.26 (s, 3H), 1.56 (s, 3H), 1.66 (br, 1H), 2.57 (s, 3H), 2.74 (t, J = 6.9 Hz, 2H), 2.89-3.00 (m, 2H), 3.1 (br, 1H), 3.60 (d, J = 10.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 5.95 (ABq, 2H), 6.66-6.77 (m, 3H), 7.15 (s, 1H), 7.26 (s, 1H), 7.83 (s, 1H)

MS (ESI⁺) m / z; 441 [M+1]⁺

Synthesis Example 30

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(1-piperidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol

(Yield: 61%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.29 (s, 3H), 1.58 (s, 3H), 1.60 (br s, 2H), 1.50-1.70 (m, 6H), 2.30-2.60 (m, 6H), 2,58 (s, 3H), 3.06 (t, J = 5.8 Hz, 2H), 3.54 (d, J = 10.4 Hz, 1H),

3.80 (d, J = 10.4 Hz, 1H), 7.13 (s, 1H), 7.23 (s, 1H), 8.06 (s, 1H).

MS (ESI⁺) m / z; 404 [M+1]⁺

MS (ESI) m / z; 448 [M+45]* (HCOOH adduct)

Synthesis Example 31

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}-3,4-dihyd ro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 55%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.29 (s, 3H), 1.58 (s, 3H), 1.49-2.00 (m, 8H), 2.10-2.25 (m, 2H), 2.34 (s, 1.5H), 2.35 (s, 1.5H), 2.58 (s, 3H), 2.65-2.85 (m, 2H), 3.00-3.15 (m, 1H), 3.62 (d, J = 10.4 Hz, 0.5H), 3.70 (d, J = 10.4 Hz, 0.5H), 3.85 (d, J = 10.4 Hz, 0.5H), 7.15 (s, 1H), 7.27 (s, 1H), 7.96 (s, 1H).

MS (ESI⁺) m / z; 404 [M+1]⁺

MS (ESI⁻) m / z; 448 [M+45]⁺ (HCOOH adduct)

Synthesis Example 32

 $(3R^*,4S^*)$ -4-[(2-anilinoethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 78%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.27 (s, 3H), 1.56 (s, 3H), 1.77 (br s, 3H), 2.58 (s, 3H), 2.95-3.10 (m, 2H), 3.30 (t, J = 5.5 Hz, 2H), 3.64 (d, J = 10.2 Hz, 1H), 3.93 (d, J = 10.2 Hz, 1H), 6.65-6.80 (m, 3H), 7.15-7.20 (m, 3H), 7.28 (s, 1H), 7.98 (s, 1H).

MS (ESI⁺) m / z; 412 [M+1]⁺

MS (ESI) m / z; 456 $[M+45]^+$ (HCOOH adduct)

Synthesis Example 33

 $(3R^*,4S^*)$ -7-chloro-4- $(\{2-[ethyl(3-methylphenyl)amino]ethyl\}amino)$ -2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 90%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.23 (t, J = 6.9 Hz, 3H), 1.26 (s, 3H), 1.55 (s, 3H), 1.62 (br s, 1H), 2.27 (s, 3H), 2.57 (s, 3H), 2.80-3.00 (m, 2H), 3.30-3.50 (m, 5H), 3.61 (d, J = 10.1 Hz, 1H), 3.91 (d, J = 10.1 Hz, 1H), 6.60-6.70 (m, 4H), 7.05-7.15 (m, 2H), 7.96 (s, 1H).

MS (ESI⁺) m / z; 454 [M+1]⁺ MS (ESI⁻) m / z; 498 [M+45]⁺ (HCOOH adduct)

Synthesis Example 34

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[(1-ethyl-(R)-2-pyrrolidinyl)methyl]amino}-3,4-dih ydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 93%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.27 (s, 1H), 1.32 (t, J = 7.1 Hz, 2H), 1.56 (s, 3H), 1.9**5**-2.12 (br, 4H),2.56 (s, 3H), 2.71-2.81 (br, 2H), 2.98-3.37 (m, 4H), 3.64-4.01 (m, 5H), **7**.12 (s, 1H), 7.22 (s, 1H), 8.01 (s, 1H)

MS (ESI⁺) m / z; 405 [M+1]⁺

MS (ESI⁻) m / z; 448 [M+45]⁺ (HCOOH adduct)

Synthesis Example 35

 $(3R^*,4S^*)$ -7-chloro-4-[(2,2-diethoxyethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano [2,3-g]quinolin-3-ol maleate

(Yield: 88%)

White solid

¹H-NMR (CD₃OD) δ: 1.23-1.30 (m, 9H), 1.57 (s, 3H), 2.64 (s, 3H), 3.50-3.85 (m, 4H), 4.02 (d, J = 10.2 Hz, 1H), 6.27 (s, 1H), 7.37 (s, 1H), 7.49 (s, 1H), 8.13 (s, 1H)

Free form

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-[(2,2-diethoxyethyl)amino]-3,4-dihydro-2*H*-pyrano [2,3-g]quinolin-3-ol

Pale yellow amorphous product

MS (ESI⁺) m / z; 410 [M+1]⁺

MS (ESI⁻) m / z; 453 [M+45]⁺ (HCOOH adduct)

Synthesis Example 36

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(3-thienyl)ethyl]amino}-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 57%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.24 (s, 3H), 1.55 (s, 3H), 2.56 (s, 3H), 2.84 (t, J = 6.8 Hz, 2H), 2.90-3.09 (m, 2H), 3.60 (d, J = 10.5 Hz, 1H), 3.86 (d, J = 10.5 Hz, 1H), 6.94-7.01 (m,

2H), 7.13 (s, 1H), 7.24-7.29 (m, 2H), 7.89 (s, 1H) MS (ESI⁺) m / z; 404 [M+1]⁺ MS (ESI⁻) m / z; 447 [M+45]⁺ (HCOOH adduct)

Synthesis Example 37

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-[2-(1-pyrazolylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 59%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.58 (s, 3H), 1.86 (br s, 1H), 2.57 (s, 3H), 3.26-3.31 (m, 2H), 3.63 (d, J = 10.1 Hz, 1H), 3.87 (d, J = 10.1 Hz, 1H), 4.24-4.32 (m, 2H), 5.00 (br s, 1H), 6.32 (dd, J = 1.7, 3.4 Hz, 1H), 7.14 (s, 1H), 7.25 (s, 1H), 7.45 (d, J = 1.7 Hz, 1H), 7.58 (d, J = 1.7 Hz, 1H), 8.00 (s, 1H) MS (ESI⁺) m / z; 387 [M+1]⁺

Synthesis Example 38

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(4-methylpyrazol-1-yl)ethyl]amino}-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 70%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.58 (s, 3H), 2.00 (br s, 1H), 2.10 (s, 3H), 2.5**7** (s, 3H), 3.16-3.31 (m, 2H), 3.64 (d, J = 10.2 Hz, 1H), 3.87 (d, J = 10.2 Hz, 1H), 4.1**1**-4.30 (m, 2H), 5.20 (br s, 1H), 7.13 (s, 1H), 7.21 (s, 1H), 7.24 (s, 1H), 7.36 (s, 1H), 7.98 (s, 1H)

MS (ESI⁺) m / z; 401 [M+1]⁺

Synthesis Example 39

 $(3R^*,4S^*)$ -7-chloro-4-{[2-(4-chloropyrazol-1-yl)ethyl]amino}-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 89%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.58 (s, 3H), 1.84 (br s, 1H), 2.58 (s, 3H), 3.26-3.29 (m, 2H), 3.61 (d, J = 10.4 Hz, 1H), 3.87 (d, J = 10.4 Hz, 1H), 4.16-4.29 (m, 2H), 4.51 (br s, 1H), 7.15 (s, 1H), 7.26 (s, 1H), 7.45 (s, 1H), 7.48 (s, 1H), 7.97 (s, 1H) MS (ESI⁺) m / z; 421 [M+1]⁺

Synthesis Example 40

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(2-pyridy)lethyl]amino}-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 83%)

Yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.32 (s, 3H), 1.61 (s, 3H), 1.82 (br s, 1H), 2.57 (s, 3H), 2.92-3.12 (m, 2H), 3.26-3.30 (m, 2H), 3.74 (d, J = 10.2 Hz, 1H), 3.92 (d, J = 10.2 Hz, 1H), 7.13 (s, 1H), 7.17-7.27 (m, 3H), 7.64-7.70 (m, 1H), 8.06 (s, 1H), 8.56 (d, J = 5.0 Hz, 1H) MS (ESI⁺) m / z; 398 [M+1]⁺

Synthesis Example 41

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(3-pyridyl)ethyl]amino}-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 61%)

Brown amorphous product

¹H-NMR (CDCl₃) δ: 1.26 (s, 3H), 1.55 (s, 3H), 1.73 (br s, 1H), 2.58 (s, 3H), 2.80-2.85 (m, 2H), 2.92-3.07 (m, 2H), 3.23 (br s, 1H), 3.61 (d, J = 10.4 Hz, 1H), 3.89 (d, J = 10.4 Hz, 1H), 7.16 (s, 1H), 7.22-7.27 (m, 2H), 7.55 (d, J = 7.7 Hz, 1H), 7.93 (s, 1H), 8.47-8.48 (m, 2H)

 $MS (ESI^{+}) m / z; 398 [M+1]^{+}$

Synthesis Example 42

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(4-pyridyl)ethyl]amino}-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 47%)

Pale brown amorphous product

¹H-NMR (CDCl₃) δ: 1.26 (s, 3H), 1.55 (s, 3H), 1.89 (br s, 1H), 2.58 (s, 3H), 2.80-2.85 (m, 2H), 2.94-3.11 (m, 2H), 3.60 (br s, 1H)), 3.63 (d, J = 10.4 Hz, 1H), 3.90 (d, J = 10.4 Hz, 1H), 7.15 (d, J = 5.7 Hz, 1H), 7.16 (s, 1H), 7.27 (s, 1H), 7.96 (s, 1H), 8.47 (d, J = 5.7 Hz, 2H)

MS (ESI⁺) m / z; 398 [M+1]⁺

Synthesis Example 43

(3R*,4S*)-7-chloro-4-ethylamino-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-

3-ol

(Yield: 95%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 1.18 (t, J = 7.1 Hz, 3H), 1.29 (s, 3H), 1.58 (s, 3H), 2.58 (s, 3H), 2.68-2.91 (m, 2H), 3.63 (d, J = 10.4 Hz, 1H), 3.87 (dd, J = 10.4, 1.2 Hz, 1H), 7.15 (d, J = 1.1 Hz, 1H), 7.27 (s, 1H), 7.93 (d, J = 1.1 Hz, 1H). MS (ESI⁺) m / z; 321 [M+1]⁺

Synthesis Example 44

(3R*,4S*)-7-chloro-4-isobutylamino-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinol in-3-ol

(Yield: 96%)

Pale brown amorphous product

¹H-NMR (CDCl₃) δ: 0.94-0.98 (m, 6H), 1.29 (s, 3H), 1.58 (s, 3H), 1.68-1.76 (m, 1H), 2.50-2.62 (m, 2H), 2.58 (s, 3H), 3.36 (br s, 1H), 3.63 (d, J = 10.2 Hz, 1H), 3.88 (dd, J = 10.2, 1.1 Hz, 1H), 7.15 (s, 1H), 7.28 (s, 1H), 7.93 (s, 1H) MS (ESI⁺) m / z; 239 [M+1]⁺

Synthesis Example 45

 $(3R^*,4S^*)$ -7-chloro-4-[(cyclopropylmethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2H-pyran o[2,3-g]quinolin-3-ol

(Yield: 85%)

Pale brown amorphous product

¹H-NMR (CDCl₃) δ: 0.13-0.20 (m, 2H), 0.48-0.54 (m, 2H), 0.95-1.01 (m, 1H), 1.29 (s, 3H), 1.58 (s, 3H), 1.8 (br s, 1H), 2.53 (m, 1H), 2.58 (s, 3H), 2.70 (m, 1H), 3.63 (d, J = 10.4 Hz, 1H), 3.91 (d, J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.90 (s, 1H) MS (ESI⁺) m / z; 347 [M+1]⁺

Synthesis Example 46

 $(3R^*,4S^*)$ -7-chloro-4-isopentylamino-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quin olin-3-ol

(Yield: 64%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 0.90 (d, 6H), 1.29 (s, 3H), 1.39-1.46 (m, 2H), 1.58 (s, 3H), 1.62-1.74 (m, 2H), 2.58 (s, 3H), 2.64-2.85 (m, 2H), 3.64 (d, J = 10.4 Hz, 1H), 3.87 (d,

J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.28 (s, 1H), 7.93 (s, 1H)MS (ESI⁺) m / z; 363 [M+1]⁺

Synthesis Example 47

 $(3R^*,4S^*)$ -7-chloro-4-[2-(cyclopentylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2H-pyran o[2,3-g]quinolin-3-ol

(Yield: 78%)

Pale yellow solid

¹H-NMR (CDCl₃) δ: 1.08-1.11 (m, 2H), 1.29 (s, 3H), 1.49-1.62 (m, 6H), 1.54 (s, 3H), 1.71-1.83 (m, 3H), 2.58 (s, 3H), 2.67-2.82 (m, 2H), 3.63 (d, J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.93 (s, 1H) MS (ESI⁺) m / z; 389 [M+1]⁺

Synthesis Example 48

 $(3R^*,4S^*)$ -7-chloro-4- $\{[2-(1-cyclopentenyl)ethyl]amino]\}$ -2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 70%)

Pale brown amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.58 (s, 3H), 1.86-1.94 (m, 2H), 2.22-2.34 (m, 7H), 2.58 (s, 3H), 2.79-2.96 (m, 2H), 3.63 (d, J = 10.5 Hz, 1H), 3.87 (dd, J = 10.5, 1.2 Hz, 1H), 5.44 (s, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.92 (s, 1H) MS (ESI⁺) m / z; 387 [M+1]⁺

Synthesis Example 49

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-[(5-methylhexane-2-yl)amino]-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol

(Yield: 83%)

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 0.91 (dd, J = 6.6 Hz, 9.6Hz,6H), 1.13-1.34 (m, 9H), 1.56 (s, 6H), 2.57 (s, 3H), 3.22-3.44 (m, 2H), 3.80-3.85 (br s, 1H), 7.14 (s, 1H), 7.26 (s, 1H), 7.96-7.98 (br s, 1H)

MS (ESI⁺) m / z; 392 [M+2]⁺

MS (ESI⁻) m / z; 435 [M+45]⁺ (HCOOH adduct)

Synthesis Example 50

(3S*,4R*)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3 -g]quinolin-3-ol 1 maleate

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

This compound was synthesized by using the enantiomer of Ph,Ph salen manganese complex (XX) (hereinafter, referred to as ent-Ph,Ph salen manganese complex).

(3S*,4S*)-7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoline

To a solution of 7-chloro-2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline (200 mg, 0.77 mmol) in ethyl acetate (3.0 mL), *N*-methyl imidazole (0.012 mL, 0.154 mmol) and ent-Ph,Ph salen manganese complex (8.0 mg, 0.0077 mmol) were added at room temperature and aqueous sodium hypochlorite solution (1.0 g, 1.513 mol/kg, 1.54 mmol) was added dropwise, and the resulting mixture was stirred for 40 minutes. Aqueous sodium hypochlorite solution (1.0 g, 1.513 mol/kg, 1.54 mmol) was added dropwise, and the resulting mixture was further stirred at room temperature for 30 minutes. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, the resulting solution was filtered through celite and extracted. The organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 10/1) to obtain

 $(3S^*,4S^*)$ -7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (yield: 94%).

> 99.9% ee; CHIRALCEL OJ-R acetonitrile/methanol/0.01 M aqueous sodium chloride solution = 1/3/3, Retention time: 44.3 min.

 $(3S^*,4R^*)$ -7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3]

-g]quinolin-3-ol 1 maleate

To a solution of

(3S*,4S*)-7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (199 mg, 0.72 mmol) in 1,4-dioxane (0.4 mL), lithium perchlorate (77.0 mg, 0.72 mmol) and 2-phenylethylamine (0.11 mL, 0.87 mmol) were added at room temperature and the resulting mixture was stirred at 70°C for 3 hours. Upon the completion of the reaction, aqueous sodium hydrogencarbonate solution was added to the reaction solution, and it was extracted with ethyl acetate and the resulting organic phase was washed with aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 3/1). Further, after distilling off the solvent, ethyl acetate (2 mL) was added and a solution of maleic acid (50.3 mg, 0.43 mmol) in ethyl acetate (2mL) was added dropwise. The precipitated solid was filtered to obtain

(3S*,4R*)-7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3 -g]quinolin-3-ol 1 maleate (yield: 41%).

White crystals

mp: 240-242°C

¹H-NMR(DMSO-d₆): 1.18(s, 3H), 1.50(s, 3H), 2.60(s, 3H), 2.97-3.32(m, 4H), 4.04-4.09(m, 1H), 4.65(d, J = 9.6 Hz, 1H), 6.05(s, 2H), 6.29(br s, 1H), 7.23-7.35(m,

5H), 7.44(s, 2H), 8.32(s, 1H)

MS(ESI*)m/z; 397 [M+1] *

MS(ESI⁻)m/z; 441 [M+45] + (HCOOH adduct)

Synthesis Example 51

 $(3S^*,4R^*)$ -2,2,7,9-tetramethyl-4-[(2-pentylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]qu inolin-3-ol 1 maleate

This compound was synthesized according to the process of Synthesis Example 50.

(2-steps yield: 25%)

epoxy 99.1%ee CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile =

60/40, Retention time: 10.3 min.

White crystals

mp: 215-216°C (decomposition)

¹H-NMR(DMSO-d₆); 1.16(s, 3H), 1.49(s, 3H), 2.55(s, 3H), 2.58(s, 3H), 2.97-3.32 (m, 4H), 4.02-4.04(m, 1H), 4.62(br s, 1H), 6.04(s, 2H), 6.25(br s, 1H), 7.24-7.36(m, 7H), 8.31(s, 1H)

MS(ESI⁺)m/z; 377 [M+1] +

Synthesis Example 52

(3R*,4S*)-7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol hydrochloride

(3R*,4S*)-4-amino-7-chloro-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

To a solution of

 $(3R^*,4R^*)$ -7-chloro-3,4-epoxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline (2.0 g, 7.25 mmol) in ethanol (20 mL), ammonia water (10 mL) was added, and the resulting mixture was stirred in a sealed tube at 90°C for 3 hours. Upon the completion of the reaction, the reaction solution was concentrated, and ethyl acetate was added thereto, The resulting solution was washed with water and then with saturated sodium chloride solution, and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/2) to obtain the aimed product (yield: 86%).

White crystals

¹H-NMR(CDCl₃) δ; 1.30 (s, 3H), 1.58 (s, 3H), 1.67 (br s, 2H), 2.59 (s, 3H), 3.28 (br s, 1H), 3.45 (d, J = 10.4 Hz, 1H), 3.85 (d, J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.26 (s, 1H), 8.02 (s, 1H).

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinolin

-3-ol

To a solution of

(3R*,4S*)-4-amino-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (60 mg, 0.205 mmol) in methanol (1.2 mL), butyl aldehyde (35 mg, 0.041 mmol) was added, and the resulting mixture was stirred at room temperature for 20 minutes. Sodium cyanoborohydride (52 mg, 0.82 mmol) was added thereto, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, and the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 3/1) to obtain the aimed product (yield: 41%).

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 0.90 (t, J = 6.9 Hz, 3H), 1.29 (s, 3H), 1.20-1.45 (m, 4H), 1.55-1.70 (m, 4H), 2.58 (s, 3H), 2.60-2.82 (m, 2H), 3.63 (d, J = 10.4 Hz, 1H), 3.86 (d, J =10.4 Hz, 1H), 7.15 (s, 1H), 7.28 (s, 1H), 7.93 (s, 1H).

MS (ESI⁺) m / z; 363 [M+1]⁺

MS (ESI) m / z; 407 [M+45] (HCOOH adduct)

(3R*,4S*)-7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol hydrochloride

To a solution of

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin -3-ol (28 mg, 0.77 mmol) in ether (560 μ L), 4 M hydrogen chloride solution in ether (56 μ L) was added dropwise, and the resulting mixture was stirred at 0°C for 15 minutes. Solid product was filtered off, washed with ether and dried to obtain the aimed product (yield: 88%).

Colorless crystals

mp: 291-294°C (decomposition)

Synthesis Examples 53-57

The compounds of Synthesis Examples 53-57 were synthesized according to the process of Synthesis Example 52.

Synthesis Example 53

 $(3R^*,4S^*)$ -7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2H-pyrano [2,3-g]quinolin-3-ol hydrochloride

Free form

 $(3R^*,4S^*)$ -7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano [2,3-g]quinolin-3-ol

(Yield: 31%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 0.90-1.00 (m, 2H), 1.05-1.25 (m, 6H), 1.29 (s, 3H), 1.58 (s, 3H)1.60-1.70 (m, 7H), 2.58 (s, 3H), 2.75-2.85 (m, 2H), 3.63 (d, J = 10.4 Hz, 1H), 3.86 (d, J = 10.4 Hz, 1H), 7.15 (s, 1H), 7.27 (s, 1H), 7.93 (s, 1H)

Hydrochloride

(3R*,4S*)-7-chloro-4-[(2-cyclohexylethyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano [2,3-g]quinolin-3-ol hydrochloride

(Yield: 76%)

Colorless crystals

mp: 294-295°C (decomposition)

MS (ESI⁺) m / z; 403 [M+1]⁺

MS (ESI⁻) m / z; 447 [M+45]⁺ (HCOOH adduct)

Synthesis Example 54

 $(3R^*,4S^*)$ -7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol hydrochloride

Free form

(3R*,4S*)-7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 65%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.29 (s, 3H), 1.20-1.40 (m, 4H), 1.58 (s, 3H), 1.50-1.80 (m, 4H), 2.59 (s, 3H), 2.65-2.90 (s, 2H), 3.20-3.40 (m, 3H), 3.64 (d, J = 10.4 Hz, 1H), 3.70-3.75 (m, 1H), 3.85 (d, J = 10.4 Hz, 1H), 3.80-4.00 (m, 3H), 7.16 (s, 1H), 7.28 (s, 1H), 7.92 (s, 1H).

MS (ESI⁺) m / z; 405 [M+1]⁺

MS (ESI⁻) m / z; 449 [M+45]⁺ (HCOOH adduct)

Hydrochloride

 $(3R^*,4S^*)$ -7-chloro-4-[{2-(tetrahydropyran-4-yl)ethyl}amino]-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol hydrochloride

(Yield: 72%)

Colorless crystals

mp: 318-320°C (decomposition)

Synthesis Example 55

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-[{2-(4-thianyl)ethyl}amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

(Yield: 63%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.40-1.60 (m, 5H), 1.56 (s, 1H), 1.90-2.00 (m, 2H), 2.59 (s, 3H), 2.50-2.85 (m, 6H), 3.23 (s, 1H), 3.63 (d, J = 10.4 Hz, 1H), 3.87 (d, J = 10.4 Hz, 1H), 7.16 (s, 1H), 7.28 (s, 1H), 7.91 (s, 1H).

MS (ESI⁺) m / z; 421 [M+1]⁺

MS (ESI⁻) m / z; 465 [M+45]⁺ (HCOOH adduct)

Synthesis Example 56

 $(3R^*,4S^*)$ -7-chloro-4- $(\{[6-(4-chlorophenyl)-3-pyridinyl]methyl\}amino)-2,2,9-trimethyl-3, 4-dihydro-2<math>H$ -pyrano[2,3-g]quinolin-3-ol hydrochloride

Free form

 $(3R^*,4S^*)$ -7-chloro-4-({[6-(4-chlorophenyl)-3-pyridinyl]methyl}amino)-2,2,9-trimethyl-3, 4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 16%)

¹H-NMR (CDCl₃) δ: 1.30 (s, 3H), 1.59 (s, 3H), 1.60 (br s, 1H), 2.60 (s, 3H), 2.98 (s, 1H), 3.75-4.10 (m, 4H), 7.19 (s, 1H), 7.34 (s, 1H), 7.45 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 9.0 Hz, 1H), 7.80 (dd, J = 9.0, 2.2Hz, 1H), 7.96 (d, J = 8.8 Hz, 2H), 8.09 (s, 1H), 8.66 (d, J = 2.2 Hz, 1H).

 $MS (ESI^{+}) m / z; 494[M+1]^{+}$

MS (ESI') m / z; 538 [M+45]⁺ (HCOOH adduct)

Hydrochloride

 $(3R^*,4S^*)$ -7-chloro-4- $(\{[6-(4-chlorophenyl)-3-pyridinyl]methyl\}amino)-2,2,9-trimethyl-3, 4-dihydro-2<math>H$ -pyrano[2,3-g]quinolin-3-ol hydrochloride

(Yield: 67%)

Pale yellow solid

Synthesis Example 57

 $(3R^*,4S^*)$ -4-[(2-benzofurylmethyl)amino]-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyra no[2,3-g]quinolin-3-ol

(Yield: 74%)

Colorless amorphous product

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.58 (s, 3H), 2.0 (br), 2.59 (s, 3H), 3.35 (br, 1H), 3.75 (d, J = 10.2 Hz, 1H), 4.04 (dd, J = 10.2, 1.1 Hz, 1H), 4.06 (s, 2H), 6.60 (s, 1H), 7.16 (s, 1H), 7.18-7.27 (m, 2H), 7.30 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.49-7.52 (m, 1H), 8.08 (d, J = 1.1 Hz, 1H)

MS (ESI⁺) m / z; 423 [M+1]⁺

Synthesis Example 58

 $(3R^*,4S^*)$ -7-chloro-4-[(2-hydroxypentyl)amino]-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol

Under nitrogen stream, 1,2-epoxypentane (71 μ L, 0.682 mmol) was added to a solution of

 $(3R^*,4S^*)$ -4-amino-7-chloro-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol (100 mg, 0.343 mmol) and lithium perchlorate (36 mg, 0.343 mmol) in dioxane (0.50 mL) at room temperature, and the resulting mixture was stirred at 70°C for 25 hours. Upon the completion of the reaction, ethyl acetate was added thereto, the resulting reaction solution was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated aqueous sodium chloride solution, and then dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) to obtain the aimed product (yield: 59%).

Pale yellow amorphous product

¹H-NMR (CDCl₃) δ: 0.93 (t, J = 6.9 Hz, 3H), 1.28 (s, 3H), 1.30-1.50 (m, 4H), 1.57 (s, 3H), 1.91 (br s, 3H), 2.59 (s, 3H), 2.60-2.70 (m, 1H), 2.85-3.00 (m, 1H), 3.60-3.75 (m, 2H), 3.90-4.00 (m, 1H), 7.16 (s, 1H), 7.28 (s, 1H), 7.99 (s, 0.5H), 8.00 (s, 0.5H). MS (ESI⁺) m / z; 379 [M+1]⁺

MS (ESI⁻) m / z; 423 [M+45]⁺ (HCOOH adduct)

Synthesis Example 59

 $(3R^*,4S^*)$ -2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoxal in-3-ol 1 maleate

 $(3R^*,4S^*)$ -6,7-diamino-3,4-dihydro-2,2-dimethyl-4-(2-phenylethylamino)-2H-1-benzop

yran-3-ol

$$H_2N$$
 H_2N
 O
 O

Under hydrogen stream at 1 atm, a solution of

(*3R**, *4S**)-6-amino-3,4-dihydro-2,2-dimethyl-7-nitro-4-(2-phenylethylamino)-2*H*-benzo pyran-3-ol (10.0 g, 28.0 mmol) and 5% palladium carbon (AER type, 1 g) in ethanol (200 mL) was stirred at room temperature for 6 hours. Upon the completion of the reaction, the reaction solution was filtered through celite and concentrated to obtain the aimed product (yield: 98%).

Black amorphous product

¹H-NMR (CDCl₃) δ: 1.13 (s, 3H), 1.43 (s, 3H), 2.60-3.0 (m, 4H), 2.5-3.5 (br, 6H), 3.47 (d, J = 9.6 Hz, 1H), 3.51 (d, J = 9.6 Hz, 1H), 6.12 (s, 1H), 6.14 (s, 1H), 7.15-7.50 (m, 5H)

MS (ESI) m / z; $400[M+1]^+$, 327 (bp).

 $(3R^*,4S^*)$ -2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoxal in-3-ol

To a solution of

 $(3R^*,4S^*)$ -6,7-diamino-3,4-dihydro-2,2-dimethyl-4-(2-phenylethylamino)-2*H*-benzopyr an-3-ol (1.5 g, 4.58 mmol) in ethanol (30 mL), 40% aqueous glyoxal solution (997 mg, 6.87 mmol) was added, and the resulting mixture was stirred at room temperature for 30 minutes. Upon the completion of the reaction, ethyl acetate was added thereto, the resulting solution was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, and then dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) to obtain the aimed product (yield: 74%).

1H-NMR (CDCl₃) δ : 1.26 (s, 3H), 1.56 (s, 3H), 1.60 (br s, 1H), 2.86 (t, J = 6.9 Hz, 1H), 2.90-3.10 (m, 3H), 3.62 (d, J = 10.4 Hz, 1H), 3.90 (d, J = 10.4 Hz, 1H), 7.24-7.40 (m, 5H), 7.42 (s, 1H), 7.94 (s, 1H), 8.05 (d, J = 1.7 Hz, 1H), 8.72 (d, J = 1.7 Hz, 1H)

MS (ESI⁺) m / z; 350 [M+1]⁺ MS (ESI⁻) m / z; 349 [M-1]⁺

(3R*,4S*)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoxal in-3-ol 1 maleate

To a solution of

(3R*,4S*)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxal in-3-ol (1.18 g, 3.38 mmol) in ethyl acetate (22 mL), maleic acid (471 mg, 4.06 mmol) was added at room temperature, and the resulting mixture was stirred for 10 minutes. Upon the completion of the reaction, solid product was filtered off, washed with ethyl acetate and dried to obtain the aimed product (yield: 61%).

Pale gray crystals

mp: 176-179°C (decomposition)

¹H-NMR (DMSO-d₆) δ: 1.20 (s, 3H), 1.52 (s, 3H), 2.90-3.70 (m, 6H), 4.00-4.15 (m, 1H), 4.71 (d, J = 9.1 Hz, 1H), 6.07 (s, 2H), 6.34 (br s, 1H), 7.15-7.45 (m, 5H), 7.43 (s, 1H), 8.50 (s, 1H), 8.84 (s, 1H), 8.88 (s, 1H).

Synthesis Example 60

 $(3R^*,4S^*)$ -4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride

Synthesis Example 60 was carried out similarly to the process of Synthesis Example 59.

 $(3R^*, 4S^*)$ -6,7-diamino-4-[{2-(2-fluorophenyl)ethyl}amino]-2,2-dimethyl-3,4-dihydro-2*H*-benzopyran-3-ol

$$H_2N$$
 O
 O
 O

(Yield: 87%)

Black amorphous product

MS (ESI⁺) m / z; 346 [M+1]⁺

MS (ESI⁻) m / z; 380 [M+45]⁺ (HCOOH adduct)

 $(3R^*,4S^*)$ -4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol

(Yield: 25%)

Gray amorphous product

¹H–NMR (CDCl₃) δ: 1.26 (s, 3H), 1.57 (s, 3H), 1.74 (br s, 2H), 2.85-3.15 (m, 4H), 3.61 (d, J = 10.4 Hz, 1H), 3.91 (d, J = 10.4 Hz, 1H), 7.00-7.15 (m, 3H), 7.15-7.35 (m, 2H), 7.42 (s, 1H), 7.98 (s, 1H), 8.66 (d, J = 1.7 Hz, 1H), 8.72 (d, J = 1.7 Hz, 1H).

MS (ESI⁺) m / z; 368 [M+1]⁺

MS (ESI⁻) m / z; 412 [M+45]⁺ (HCOOH adduct)

 $(3R^*,4S^*)$ -4-{[2-(2-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride

(Yield: 95%)

Colorless crystals

mp: 265-268°C (decomposition)

Synthesis Example 61

 $(3R^*,4S^*)$ -4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol hydrochloride

Synthesis Example 61 was carried out similarly to the process of Synthesis

Example 59.

 $(3R^*,4S^*)$ -6,7-diamino-4-[{2-(4-fluorophenyl)ethyl}amino]-2,2-dimethyl-3,4-dihydro -2H-1-benzopyran-3-ol

$$H_2N$$
 O
 O
 O
 O
 O

(Yield: 87%)

Black amorphous product

¹H-NMR (CDCl₃) δ: 1.13 (s, 3H), 1.45 (s, 3H), 1.90 (br s, 4H), 2.75-3.00 (m, 6H), 3.50-3.70 (m, 2H), 6.16 (s, 1H), 6.29 (s, 1H), 7.02 (t, J = 8.5 Hz, 2H), 7.17 (t, J = 8.5 Hz, 2H).

 $(3R^*,4S^*)$ -4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol

(Yield: 23%)

Pink oily product

¹H-NMR (CDCl₃) δ: 1.27 (s, 3H), 1.57 (s, 3H), 1.69 (br s, 2H), 2.83 (t, J = 6.9 Hz, 2H), 2.90-3.10 (m, 4H), 3.64 (d, J = 10.4 Hz, 1H), 3.92 (d, J = 10.4 Hz, 1H), 6.95-7.05 (m, 2H), 7.15-7.25 (m, 2H), 7.42 (s, 1H), 7.94 (s, 1H), 8.66 (d, J = 1.7 Hz, 1H), 8.73 (d, J = 1.7 Hz, 1H).

(8R*,9S*)-{[2-(4-fluorophenyl)ethyl]amino}-7,7-dimethyl-8,9-dihydro-7*H*-pyrano[2,3-g]q uinoxalin-8-ol hydrochloride

(Yield: 95%)

Brown crystals

mp: 191-197°C (decomposition)

Synthesis Example 62

(3R*,4S*)-4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3 -g]quinoxalin-3-ol

Synthesis Example 62 was carried out similarly to the process of Synthesis Example 59.

(3R*,4S*)-6,7-diamino-4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2 H-1-benzopyran-3-ol

$$H_2N$$
 H_2N
 O
 O

(Yield: 92%)

Two diastereomers that can not be separated

Black amorphous product

¹H-NMR (CDCl₃) δ: 1.16 (s, 3H), 1.43 (s, 3H), 2.31 (br s, 7H), 2.70-3.05 (m, 3H), 3.50-3.70 (m, 2H), 4.70-4.80 (m, 1H), 6.16 (s, 1H), 6.53 (s, 0.5H), 6.58 (s, 0.5H), 7.20-7.40 (s, 5H).

(3R*,4S*)-4-[(2-hydroxy-2-phenylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3 -g]quinoxalin-3-ol

(Yield: 66%)

Two diastereomers that can not be divided

Gray amorphous product

¹H-NMR (CDCl₃) δ: 1.30 (s, 3H), 1.58 (s, 1.5H), 1.59 (s, 1.5H), 1.70 (br s, 3H), 2.90-3.10 (m, 2H), 3.71 (d, J = 10.5Hz, 1H), 3.95-4.05 (m, 1H), 7.20-7.45 (m, 6H), 8.10(s, 0.5H), 8.12 (s, 0.5H), 8.64 (d, J = 1.9 Hz, 1H), 8.73 (d, J = 1.9 Hz, 1H).

MS (ESI⁺) m / z: 366 [M+1]⁺

MS (ESI) m / z; 410 [M+45]* (HCOOH adduct)

Synthesis Example 63

 $(3R^*,4S^*)$ -2,2-dimethyl-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol hydrochloride

Synthesis Example 63 was carried out similarly to the process of Synthesis Example 59.

(3R*,4S*)-6,7-diamino-2,2-dimethyl-4-pentylamino-3,4-dihydro-2H-1-benzopyran-3-ol

$$H_2N$$
 O O O O

(Yield: 98%)

Brown amorphous product

¹H-NMR (CDCl₃) δ: 0.80-0.90 (m, 3H), 0.99 (s, 3H), 1.26 (s, 3H), 1.30-1.50 (m, 5H), 2.20-2.30 (m, 1H), 2.40-2.50 (m, 4H), 3.30-3.60 (m, 4H), 3.90 (br s, 2H), 4.34 (br s, 2H), 4.93 (d, J = 4.4 Hz, 1H), 5.89 (s, 1H), 6.59 (s, 1H).

 $(3R^*,4S^*)$ -2,2-dimethyl-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol

(Yield: 36%)

Orange amorphous product

¹H-NMR (CDCl₃) δ: 0.90 (t, J =7.4 Hz, 3H), 1.32 (s, 3H), 1.20-1.40 (m, 3H), 1.60-1.70 (m, 3H), 1.61 (s, 3H), 1.81 (br s, 2H), 2.60-2.90 (m, 2H), 3.68 (d, J = 10.2Hz, 1H), 3.93 (d, J = 10.2 Hz, 1H), 7.44 (s, 1H), 8.04 (s, 1H), 8.66 (d, J = 1.9 Hz, 1H), (d, J = 1.9 Hz, 1H).

 $(3R^*,4S^*)$ -2,2-dimethyl-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol

hydrochloride

(Yield: 96%)

Pale yellow crystals

mp: 209-212°C (decomposition) MS (ESI⁺) m / z; 316 [M+1]⁺

Synthesis Example 64

(3R*,4S*)-2,2,7,8-tetramethyl-4-[(2-p henylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]q uinoxalin-3-ol maleate

Synthesis Example 64 was carried out similarly to the process of Synthesis Example 59.

 $(3R^*,4S^*)$ -2,2,7,8-tetramethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]q uinoxalin-3-ol

(Yield: 80%)

White amorphous product

¹H-NMR (CDCl₃) δ: 1.24 (s, 3H), 1.54 (s, 3H), 2.68 (s, 6H), 2.84 (t, J = 6.9 Hz, 2H), 2.90-3.10 (m, 4H), 3.59 (d, J = 10.2 Hz, 1H), 3.86 (d, J = 10.2 Hz, 1H), 7.20-7.40 (m, 6H), 7.82 (s, 1H).

MS (ESI⁺) m / z; 378 [M+1]⁺

MS (ESI) m / z; 380 [M+45]* (HCOOH adduct)

Synthesis Example 65

 $(3R^*,4S^*)$ -7,8-diethyl-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol

Synthesis Example 65 was carried out similarly to the process of Synthesis Example 59.

(Yield: 79%)

White solid

¹H-NMR (CDCl₃) δ: 1.23 (s, 3H), 1.39 (q, J = 6.6 Hz, 6H), 1.54 (s, 3H), 2.80-2.90 (m, 2H), 2.95-3.10 (m, 10H), 3.60 (d, J = 10.4 Hz, 1H), 3.85 (d, J = 10.4 Hz, 1H), 7.20-7.40 (m,6H), 7.81 (s, 1H).

MS (ESI⁺) m / z; 406 [M+1]⁺

Synthesis Example 66

 $(3R^*,4S^*)$ -2,2,8-trimethyl-7-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2, 3-g]quinoxalin-3-ol

Synthesis Example 66 was carried out similarly to the process of Synthesis Example 59.

(Yield: 33%, law polar component)

White amorphous product

¹H-NMR (CDCl₃) δ: 1.27 (s, 3H), 1.57 (s, 3H), 1.66 (br s. 2H), 2.72 (s, 3H), 2.83 (t, J = 6.9 Hz, 2H), 2.90-3.15 (m, 4H), 3.61 (d, J = 10.2 Hz, 1H), 3.88 (d, J = 10.2 Hz, 1H), 7.15-7.35 (m, 5H), 7.36 (s, 1H), 7.50-7.60 (m, 3H), 7.60-7.70 (m, 2H), 7.97 (s, 1H). MS (ESI⁺) m / z; 440 [M+1]⁺

Synthesis Example 67

 $(3R^*,4S^*)$ -2,2,7-trimethyl-8-phenyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2, 3-g]quinoxalin-3-ol

Synthesis Example 67 was carried out similarly to the process of Synthesis Example 59.

(Yield: 29%, high polar component)

¹H-NMR (CDCl₃) δ: 1.26 (s, 3H), 1.55 (s, 3H), 2.72 (s, 3H), 2.86 (t, J = 6.9 Hz, 2H), 2.95-3.12 (m, 4H), 3.62 (d, J = 10.2 Hz, 1H), 3.91 (d, J = 10.2 Hz, 1H), 7.20-7.35 (m, 5H), 7.42 (s, 1H), 7.45-7.55 (m, 3H), 7.60-7.70 (m, 2H), 7.90 (s, 1H). MS (ESI⁺) m / z; 440 [M+1]⁺

Synthesis Example 68

 $(3R^*,4S^*)$ -2,2,8-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quino xalin-3-ol 1 maleate

Synthesis Example 68 was carried out similarly to the process of Synthesis Example 59.

 $(3R^*,4S^*)$ -2,2,8-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quino xalin-3-ol

(Yield: 52%)

White amorphous product

¹H-NMR (CDCl₃) δ: 1.25 (s, 3H), 1.55 (s, 3H), 2.72 (s, 3H), 2.84 (t, J = 6.9 Hz, 2H), 2.90-3.10 (m, 4H), 3.61 (d, J = 10.4 Hz, 1H), 3.87 (d, J = 10.4 Hz, 1H), 7.15-7.40 (m, 6H), 7.89 (s, 1H), 8.54 (s, 1H).

maleate

Colorless crystals

mp: 189-192°C (decomposition)

Synthesis Example 69

 $(3R^*,4S^*)$ -4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]quin oxalin-3-ol hydrochloride

(3R*,4S*)-4-amino-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol

To a solution of

 $(3R^*,4S^*)$ -4,6,7-triamino-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-3-ol (280 mg, 1.25 mmol) in ethanol (5.6 mL), 40% aqueous glyoxal solution (226 mg, 1.56 mmol) was added, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, 1 mol/L hydrochloric acid was added thereto, the resulting solution was washed with ethyl acetate, the resulting aqueous phase was adjusted to pH 14 with 1 mol/L aqueous sodium hydroxide solution. Then, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (ethyl acetate/methanol = 10/1) to obtain the aimed product (yield: 35%).

Pale brown amorphous product

¹H-NMR (CDCl₃) δ: 1.26 (s, 3H), 1.58 (s, 3H), 2.17 (br s, 3H), 3.49 (d, J = 10.7 Hz, 1H), 3.92 (d, J = 10.7 Hz, 1H), 7.41 (s, 1H), 8.13 (s, 1H), 8.65 (s, 1H), 8.72 (s, 1H). MS (ESI⁺) m / z: 246 [M+1]⁺

(3R*,4S*)-4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol

To a solution of

 $(3R^*,4S^*)$ -4-amino-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoxalin-3-ol (100 mg, 0.408 mmol) in methanol (2 mL), cyclohexylmethyl aldehyde (103 mg, 0.816 mmol) was added, and the resulting mixture was stirred at room temperature for 20 minutes. Sodium cyanoborohydride (51 mg, 0.816 mmol) was added thereto, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution; and dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 2/1) to obtain the aimed product (yield: 48%).

Yellow oily product

¹H-NMR (CDCl₃) δ: 0.80-1.00 (m, 2H), 1.10-1.40 (m, 4H), 1.31 (s, 3H), 1.44 (t, J = 7.1 Hz, 1H), 1.60 (s, 3H), 1.65-1.80 (m, 6H), 2.65-2.90 (m, 2H), 3.68 (d, J = 10.4 Hz, 1H), 3.93 (d, J = 10.4 Hz, 1H), 7.44 (s, 1H), 8.04 (s, 1H), 8.67 (d, J = 1.9 Hz, 1H), 8.73 (d, J = 1.9 Hz, 1H).

(3R*,4S*)-4-[(2-cyclohexylethyl)amino]-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quin oxalin-3-ol hydrochloride

(Yield: 89%)

Yellow crystals

mp: 258-259°C (decomposition)

MS (ESI⁺) m / z; 356 [M+1]⁺

MS (ESI⁻) m / z; 400[M+45]⁺ (HCOOH adduct)

Synthesis Example 70

(±)-trans-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]benzimidazol-7-one,

To a solution of

(±)-trans-6,7-diamino-2,2-dimethyl-4-(2-phenylethylamino)-3,4-dihydro-2*H*-1-benzopyr an-3-ol (500 mg, 1.53 mmol) in dioxane (7 mL), 4 mol/L hydrogen chloride/dioxane solution (0.38 mL) was added, and the resulting mixture was stirred at room temperature for 15 minutes. Then, phenyl chloroformate (0.21 mL, 1.53 mmol) and triethylamine (0.21 mL, 1.53 mmol) were added thereto, and the resulting mixture was stirred at room temperature for 1 hour. Further, triethylamine (0.63 mL, 4.58 mmol) was added thereto, and the resulting mixture was stirred at room temperature for 2 hours. Upon the completion of the relaction, 1 mol/L hydrochloric acid was added thereto and thereby adjusted to pH 7-8. Thereafter, the resulting reaction solution was extracted with ethyl acetate, wash ed with saturated aqueous sodium chloride solution, and then dried over sodium sulfate and concentrated. The resulting mixture was purified by silica gel column (meth anol/chloroform = 1/20) to obtain the aimed product (yield: 40%).

Yellow amorphous product

¹H-NMR (CDCl₃) δ : 1.15 (s, 3H), 1.30-1.41 (br, 1H), 1.45 (s, 3H), 2.71-3.96 (m, 4H), 3.51 (d, J = 9.9 Hz, 1H), 3.67 (d, J = 9.9 Hz, 1H), 6.51 (s, 1H), 7.12-7.48 (m, 7H), 7.76 (s, 1H)

 $MS (ESI^{+}) m / z; 354 [M+1]^{+}$

Synthesis Example 71

(7R*,8S*)-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-diox a-4-aza-anthracene-3-one

4-(1,1-dimethyl-2-propenyloxy)anisole

To a solution of 4-methoxyphenol (15.0 g, 121 mmol) in acetonitrile (75 mL),

1,8-diazabicyclo[5.4.0]undecene (23.9 g, 157 mmol) was added under ice cooling and the resulting mixture was stirred at 0°C for 30 minutes (Solution 1). To a solution of 2-methyl-3-buten-2-ol (11.7 g, 139 mmol) in acetonitrile (75 mL), 1,8-diazabicyclo[5.4.0]undecene (23.9 g, 157 mmol) was added under ice cooling, the resulting mixture was stirred at 0°C for 30 minutes, then trifluoroacetic anhydride (25.4 g, 121 mmol) was added and the resulting mixture was stirred at 0°C for 30 minutes (Solution 2). Copper (I) chloride (36 mg, 0.36 mmol) was added to Solution 1, and then Solution 2 was added dropwise thereto over 15 minutes. Upon the conclusion of dropwise addition, the temperature was raised to room temperature, and the mixture was stirred overnight. Upon the completion of the reaction, an aqueous ammonium chloride solution was added to the reaction solution, and the solvent was distilled off under a reduced pressure. 1 mol/L aqueous hydrochloric acid solution was added to the residue, the resulting mixture was extracted with ethyl acetate, the

organic phase was washed once with 1 mol/L aqueous hydrochloric acid solution, twice with saturated aqueous sodium hydrogen carbonate solution and once with

anhydrous magnesium sulfate. After distilling off the solvent, the residue was directly

saturated sodium chloride solution. Then, the organic phase was dried over

6-methoxy-2,2-dimethyl-2H-1-benzopyran

used for the subsequent reaction.

A solution of 4-(1,1-dimethyl-2-propenyloxy)anisole in 1,2-dichlorobenzene (50 mL) was stirred at 190°C for 2 hours. Upon the completion of the reaction, the solvent was distilled off under a reduced pressure. The residue was purified by column chromatography (hexane/chloroform = 3/1) and the aimed product was obtained as red oily substance (2-step, yield: 61%).

¹H-NMR (CDCl₃) δ: 1.41 (s, 6H), 3.75 (s, 3H), 5.64 (d, J=9.9 Hz, 1H), 6.28 (d, J=9.9 Hz, 1H), 6.55 (d, J=2.7 Hz, 1H), 6.64-6.73 (m, 2H) LC/MS (ESI⁺): 191[M⁺+1]

6-methoxy-2,2-dimethyl-7-nitro-2*H*-1-benzopyran

A mixed solution of acetic acid (6.2 mL) and acetic anhydride (6.2 mL) containing 6-methoxy-2,2-dimethyl-2H-1-benzopyran (3.1 g, 16.4 mmol) was cooled with ice, nitric acid (1.37 mL, 18.0 mmol) was added dropwise and then the mixture was stirred at 0°C for 1 hour. Upon the completion of the reaction, 1 mol/L aqueous sodium hydroxide solution was added to the reaction solution, the resulting solution was extracted with ethyl acetate (150 mL). The organic phase was washed twice with 1 mol/L aqueous sodium hydroxide solution and once with saturated sodium chloride solution. Then, the organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 6/1) and the aimed product was obtained as yellow crystal (yield: 79%).

¹H-NMR (CDCl₃) δ: 1.44 (s, 6H), 3.91 (s, 3H), 5.85 (d, J=9.6 Hz, 1H), 6.33 (d, J=9.6 Hz, 1H), 6.69 (s, 1H), 7.34 (s, 1H)

LC/MS (ESI+): 236 [M++1]

(3R*, 4R*)-3,4-epoxy-6-methoxy-2,2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran

To a solution (300 mL) of acetonitrile containing 6-methoxy-2,2-dimethyl-7-nitro-2H-1-benzopyran (10.0 g, 42.5 mmol), N-methyl imidazole (0.678 mL, 8.50 mmol), Ph,Ph salen manganese complex (XX) (880 mg, 0.850 mmol) and iodosobenzene (18.7 mg, 85.0 mmol) were added at room temperature and the mixture was stirred for 2 hours. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added to the reaction solution, the resulting solution was filtered through celite. The resulting filtrate extracted with ethyl acetate. The organic phase was washed with water and sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as yellow crystal (yield: 75%, optical purity: 99.7% ee). 1 H-NMR (CDCl₃) δ : 1.26 (s, 3H), 1.58 (s, 3H), 3.53 (d, J=4.3 Hz, 1H), 3.90 (d, J=4.3 Hz, 1H), 3.95 (s, 3H), 7.08 (s, 1H), 7.33 (s, 1H)

MS (EI): 251 [M⁺]

HPLC: 18.6 min (enantiomer 24.1 min)

HPLC condition: chiralcel OJ-RH, MeCN/MeOH/0.01 M NaCl aq. = 1/3/5, 1.0 ml/min,

40°C, 256 nm

 $(3R^*,4S^*)$ -6-methoxy-2,2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-b enzopyran-3-ol

To a solution of $(3R^*, 4R^*)$ -3,4-epoxy-6-methoxy-2,

2-dimethyl-7-nitro-3,4-dihydro-2*H*-1-benzopyran (2.50 g, 9.95 mmol) in 1,4-dioxane (5.0 mL), lithium perchlorate (1.06 g, 9.95 mmol) and 2-phenylethylamine (1.50 mL, 11.9 mmol) were added at room temperature and the mixture was stirred at 80 °C for 1 hour. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 6/4) and the aimed product was obtained as orange amorphous substance (quantitative yield). 1 H-NMR (CDCl₃) δ : 1.15 (s, 3H), 1.47 (s, 3H), 2.73-2.95 (m, 4H), 3.60 (d, J=10.0 Hz, 1H), 3.68 (d, J= 10.0 Hz, 1H), 3.73 (s, 3H), 6.78 (s, 1H), 7.21-7.35 (m, 6H) MS (EI): 372[M⁺]

t-Butyl (2-phenylethyl) ($3R^*$, $4S^*$)-3-hydroxy-6-methoxy-2, 2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran-4-yl carbamate

To a solution of $(3R^*, 4S^*)$ -6-methoxy-2, 2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-3-ol (407)

mg, 1.09 mmol) and di-*t*-butyl carbonate (477 mg, 2.19 mmol) in tetrahydrofuran (6.0 mL), triethylamine (305 mL, 2.19 mmol) was added at 0 °C and the mixture was stirred at room temperature overnight. Upon the completion of the reaction, saturated aqueous sodium carbonate solution was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with 1 mol/L hydrochloric acid aqueous solution and saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as yellow amorphous substance (yield: 88%). MS (EI): 473 [M⁺+1]

t-Butyl (2-phenylethyl) (3R*,

4S*)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1- benzopyran-4-yl carbamate

A solution of *t*-butyl (2-phenylethyl) ($3R^*$, $4S^*$)-3-hydroxy-6-methoxy-2, 2-dimethyl-7-nitro-3,4-dihydro-2*H*-1-benzopyran-4-yl carbamate (1.32 g, 2.80 mmol) and 5% palladium-carbon (132 mg) in methanol (26 mL) was stirred under hydrogen atmosphere at room temperature overnight. Upon the completion of the reaction, the reaction solution was filtered through celite. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained (yield: 94%).

Colorless solid

LC/MS (ESI⁺): 443[M⁺+1]

t-Butyl (2-phenylethyl) (3R*,

4S*)-[7-(2-chloroacetylamino)-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-be nzopyran-4-yl] carbamate

To a solution of t-butyl (2-phenylethyl) ($3R^*$,

4S*)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyram-4-yl carbamate (270 mg, 0.61 mmol) in tetrahydrofuran, triethylamine (128 μL, 0.92 mmol) and chloroacetyl chloride (73 μL, 0.92 mmol) were added at room temperature and the resulting mixture was stirred at room temperature for 2.5 hours. Upon the completion of the reaction, ethanol (1mL) and saturated aqueous ammonium chloride solution were added to the reaction solution, and the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 5/1) and the aimed product was obtained (yield: 91%).

Colorless oily product

2-Chloro-N-[(3R*,

4S*)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-b⇔nzopyra n-7-yl]-acetamide

To a solution of t-butyl (2-phenylethyl) ($3R^*$,

4S*)-[7-(2-chloroacetylamino)-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-be nzopyran-4-yl carbamate (251 mg, 0.48 mmol) in methylene chloride (5 mL), borane trichloride (1M solution in methylene chloride, 2.42 mL, 2.42 mmol) was added at 0 °C, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, water was added thereto, the resulting solution was extracted with enthyl acetate, washed with saturated aqueous sodium hydrogenicarbonate solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexan e/ethyl

acetate = 2/1) and the aimed product was obtained (yield: 70%). Pale pink amorphous product

¹H-NMR (CDCl₃) δ: 1.33 (s, 3H), 1.44 (s, 3H), 2.75-3.00 (m, 4H), 3.50 (d, J = 9.6 Hz, 1H), 3.60 (d, J = 9.6 Hz, 1H), 4.23 (s, 2H), 6.58 (s, 1H), 6.83 (s, 1H), 7.20-7.35 (m, 5H), 8.47 (s, 1H).

MS (ESI⁺) m / z: 405 [M+1]⁺

MS (ESI⁻) m / z: 403 [M-1]⁺

(7R*,8S*)-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-diox a-4-aza-anthracene-3-one

To a solution of 2-chloro-N-[(3R*,

4S*)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyra n-7-yl]-acetamide (120 mg, 0.30 mmol) in methanol (1.2 mL), aqueous sodium hydroxide solution (1 mol/L, 1.5 mL) was added at room temperature, and the resulting mixture was stirred for 4 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium hydroxide solution (1 mol/L) and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 72%).

Colorless solid

¹H-NMR (CDCl₃) δ:1.14 (s, 3H), 1.44 (s, 3H), 2.75-3.00 (m, 4H), 3.47 (d, J = 9.9 Hz, 1H), 3.56 (d, J = 9.9 Hz, 1H), 4.50 (d, J = 15.4 Hz, 1H), 4.55 (d, J = 15.4 Hz, 1H), 6.27 (s, 1H), 6.68 (s, 1H), 7.20-7.35 (m, 5H), 7.74 (s, 1H).

MS (ESI⁺) m / z: 369 [M+1]⁺

MS (ESI⁻)·m / z: 367 [M-1]⁺

Synthesis Example 72

(7R*,8S*)-6,6-dimethyl-8-[(2-phenylethyl)amino]-2,3,4,6,7,8-hexahydro-1,5-dioxa-4-az a-anthracene-7-ol maleate

To a solution of

 $(7R^*,8S^*)$ -7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-diox a-4-aza-anthracene-3-one (42 mg, 0.11 mmol) in tetrahydrofuran (1.2 mL), lithium aluminum hydride (1M solution in tetrahydrofuran, 570 μ L, 0.57 mmol) was added at room temperature, and the resulting mixture was stirred at 90°C for 1.5 hour. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. Maleic acid (13 mg, 0.11 mmol) and hexane (1mL) were added to the solution of the resulting mixture in ethyl acetate (600 μ L) at room temperature, and the resulting mixture was stirred at room temperature for 15 minutes. The resulting crystal was filtered off and the aimed product was obtained (yield: 60%).

Pale brown solid

¹H-NMR (DMSO-d₆) δ: 1.04 (s, 3H), 1.36 (s, 3H), 2.85-3.30 (m, 6H), 3.80-3.85 (m, 1H), 4.11 (d, J = 4.2 Hz, 2H), 4.15-4.20 (m, 1H), 6.05 (s, 2H), 6.18 (s, 1H), 6.76 (s, 1H), 7.20-7.40 (m, 5H).

Synthesis Example 73

(7R*,8S*)-7-hydroxy-4,6,6-trimethyl-8-[(2-phanylethyl)amino]-4,6,7,8-tetrahydro-1,5-di oxa-4-aza-anthracene-3-one hydrochloride

t-Butyl (2-phenylethyl)

(*7R**,*8S**)-[7-hydroxy-6,6-dimethyl-3-oxo-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthrace ne-8-yl] carbamate

To a solution of

 $(7R^*,8S^*)$ -7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-diox a-4-aza-anthracene-3-one (150 mg, 0.41 mmol) in tetrahydrofuran (3 mL), triethylamine (85 μ L, 0.61 mmol) and di-t-butyl carbonate (178 mg, 0.81 mmol) were added at room temperature, and the resulting mixture was stirred at 90°C for 1.5 hour. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 85%).

MS (ESI⁺) m / z: 469 [M+1]⁺ MS (ESI⁻) m / z: 467 [M-1]⁺

t-Butyl (2-phenylethyl) (7R*,

8S*)-[7-hydroxy-4,6,6-trimethyl-3-oxo-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-8-yl] carbamate

To a solution of *t*-butyl (2-phenylethyl)

(7R*,8S*)-[7-hydroxy-6,6-dimethyl-3-oxo-

4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-8-yl] carbamate (106 mg, 0.23 mmol) in dimethylformamide (2 mL), potassium carbonate (79 mg, 0.57 mmol) and methyl iodide (28 μ L, 0.46 mmol) were added at room temperature, and the resulting mixture was stirred at room temperature for 4 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with

saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 2/1) and the aimed product was obtained (yield: 100%).

MS (ESI⁺) m / z: 505 [M+23]⁺ (Na adduct)

MS (ESI) m / z: 527 [M+45] (HCOOH adduct)

(7R*,8S*)-7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-di oxa-4-aza-anthracene-3-one

To a solution of *t*-butyl (2-phenylethyl) ($7R^*$,

 $8S^*$)-[7-hydroxy-4,6,6-trimethyl-3-oxo-4,6,7,8-tetrahydro-1,5-dioxa-4-aza-anthracene-8-yl] carbamate (115 mg, 0.24 mmol) in ether (2.2 mL), 4 mol/L hydrogen chloride-dioxane (500 μ L) was added at room temperature, and the resulting mixture was stirred at room temperature for 5 hours and then at 50°C for 30 minutes. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/2) and the aimed product was obtained (yield: 76%).

Colorless oily product

¹H-NMR (CDCl₃) δ: 1.17 (s, 3H), 1.47 (s, 3H), 2.75-3.00 (m, 4H), 3.29 (s, 3H), 3.49 (d, J = 9.9 Hz, 1H), 3.58 (d, J = 9.9 Hz, 1H), 4.52 (d, J = 15.1 Hz, 1H), 4.58 (d, J = 15.1 Hz, 1H), 6.42 (s, 1H), 6.68 (s, 1H), 7.20-7.35 (m, 5H).

MS (ESI⁺) m / z: 383 [M+1]⁺

MS (ESI⁻) m / z: 427 [M+45]⁺ (HCOOH adduct)

(ŻR*,

8S*)-7-hydroxy-4,6,6-trimethyl-8-[(2-phanylethyl)amino]-4,6,7,8-tetrahydro-1,5-dioxa-4 -aza-anthracene-3-one hydrochloride

To a solution of

 $(7R^*,8S^*)$ -7-hydroxy-4,6,6-trimethyl-8-[(2-phenylethyl)amino]-4,6,7,8-tetrahydro-1,5-di oxa-4-aza-anthracene-3-one (65 mg, 0.17 mmol) in ether (2.2 mL), 4 mol/L hydrogen chloride-ethene (200 μ L) was added at room temperature, and the resulting mixture was stirred at room temperature for 10 minutes. Upon the completion of the reaction, the resulting crystal was filtered off and the aimed product was obtained (yield: 93%). Pale pink solid

Synthesis Example 74

(±)-trans-7-Hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-diox a-1-aza-anthracene-2-one

2-methoxymethoxy-4-(1,1-dimethyl-2-propionyloxy)-1-nitro-benzene

To a solution of 4-fluoro-2-nitrophenol (1.6 g, 10.2 mmol) in tetrahydrofuran (32 mL), chloromethyl methyl ether (1.23 g, 15.3 mmol) and diisopropyl ethyl amine (2.66 mL, 15.3 mmol) were added at room temperature, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. Sodium hydride (553 mg, 12.3 mmol) and 1-methyl-2-butyn-1-ol (1.23 mL, 12.7 mmol) were added to the solution of the resulting mixture in dimethylacetamide (17 mL) at 0°C, and the resulting mixture was stirred for 7 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 5/1) and the aimed product was obtained (yield: 94%).

Yellow oily product

7-Methoxymethoxy-2,2-dimethyl-6-nitro-2*H*-1-benzopyran

A solution of

2-methoxymethoxy-4-(1,1-dimethyl-2-propionyloxy)-1-nitro-benzene (2.1 g, 7.92 mmol) in dichlorobenzene (21 mL) was stirred at 200°C for 0.5 hour. Upon the completion of the reaction, the resulting mixture was concentrated and purified by silica gel column (hexane/ethyl acetate = 5/1). Thereby, a mixture (1:1) of the aimed product and the positional isomer was obtained (yield: 77%).

Yellow oily product

¹H-NMR (CDCl₃) δ: 1.46 (s, 6H), 3.53 (s, 1.5 H), 3.58 (s, 1.5H), 5.10 (s, 1H), 5.27 (s, 1H), 5.64 (d, J = 10.4 Hz, 0.5H), 5.74 (d, J = 10.4 Hz, 0.5H), 6.27 (d, J = 10.4 Hz, 0.5H), 6.60-6.70 (m, 1.5H), 7.67 (s, 0.5H), 7.77 (d, J = 9.1 Hz, 0.5H).

(±)-trans-3-Bromo-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyr an-4-ol

To an aqueous solution of a mixture of

7-methoxymethoxy-2,2-dimethyl-6-nitro-2*H*-1-benzopyran and the positional isomer (1.5 g, 5.65 mmol) in dimethylsulfoxide (17 mL), *N*-bromosuccinimide (1.21 g, 6.78 mmol) was added at room temperature, and the resulting mixture was stirred for 3 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 7/1) and the aimed product was obtained (yield: 27%).

and the almed product was obtained (yield: 27%)

Yellow solid

¹H-NMR (CDCl₃) δ: 1.45 (s, 3H), 1.63 (s, 3H), 2.73 (d, J = 4.4 Hz, 1H), 3.52 (s, 3H), 4.08 (d, J = 9.4 Hz, 1H), 4.88 (dd, J = 9.4, 4.4 Hz, 1H), 6.71 (s, 1H), 8.16 (s, 1H).

3,4-Epoxy-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyran

To a solution of

(±)-trans-3-bromo-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyr an-4-ol (550 mg, 1.52 mmol) in dioxane (5.5 mL), 1 mol/L aqueous sodium hydroxide solution (1.82 mL, 1.82 mmol) was added at room temperature, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, water was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium thiosulfate solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 4/1) and the aimed product was obtained (yield: 78%).

Yellow oily product

¹H-NMR (CDCl₃) δ: 1.32 (s, 3H), 1.59 (s, 3H), 3.51 (s, 3H), 3.52 (d. J = 3.9 Hz, 1H), 3.91 (d, J = 3.9 Hz, 1H), 5.26 (s, 2H), 6.73 (s, 1H), 8.05 (s, 1H).

(±)-trans-7-Methoxymethoxy-2,2-dimethyl-6-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro -2*H*-1-benzopyran-3-ol

To a solution of

3,4-epoxy-7-methoxymethoxy-2,2-dimethyl-6-nitro-3,4-dihydro-2*H*-1-benzopyran (332 mg, 1.18 mmol) in dioxane (1.3 mL), lithium perchlorate (126 mg, 1.18 mmol) and 2-phenylethylamine (214 mg, 1.77 mmol) were added at room temperature, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, saturated aqueous sodium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 73%).

Yellow oily product

 1 H-NMR (CDCl₃) δ: 1.19 (s, 3H), 1.47 (s, 3H), 2.75-3.00 (m, 4H), 3.45-3.55 (m, 2H), 3.50 (s, 3H), 5.24 (s, 2H), 6.66 (s, 1H), 7.15-7.40 (m, 5H), 7.72 (s, 1H)

(±)-trans-6-amino-7-Methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihyd ro-2*H*-1-benzopyran-3-ol

To a solution of

(±)-trans-7-methoxymethoxy-2,2-dimethyl-6-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro -2*H*-1-benzopyran (265 mg, 0.66 mmol) in ethanol (5 mL), 5% palladium-carbon (AER type, 13 mg) was added at room temperature, and the resulting mixture was stirred under hydrogen stream overnight. Upon the completion of the reaction, the resulting solution was filtered through celite, concentrated, and the aimed product was obtained (yield: 98%).

Brown oily product

¹H-NMR (CDCl₃) δ: 1.13 (s, 3H), 1.43 (s, 3H), 2.70-3.05 (m, 8H), 3.51 (s, 3H), 3.52-3.60 (m, 2H), 5.12 (s, 2H), 6.21 (s, 1H), 6.51 (s, 1H), 7.20-7.50 (m, 5H).

2-Chloro-N-[(\pm)-trans-3-hydroxy-7-methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)am ino]-3,4-dihydro-2H-1-benzopyran-6-yl]-acetamide

То

trans-6-amino-7-Methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-3-ol (242 mg, 0.65 mmol) in ethyl acetate-dimethylformamide mixed solution (5 mL), 4 M hydrogen chloride-dioxane solution (194 μ L, 0.78 mmol) was added at 0°C, and the resulting mixture was stirred for 5 minutes. Chloroacetyl chloride (88 mg, 0.78 mmol) was added thereto, and the resulting mixture was stirred

for 15 minutes. Upon the completion of the reaction, ethanol and saturated aqueous sodium hydrogen carbonate solution were added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 79%).

Pale pink oily product

¹H-NMR (CDCl₃) δ: 1.17 (s, 3H), 1.45 (s, 3H), 2.75-3.00 (m, 4H), 3.43 (d, J = 9.9 Hz, 1H), 3.50 (s, 3H), 3.59 (d, J = 9.9 Hz, 1H), 4.20 (s, 2H), 5.19 (s, 2H), 6.61 (s, 1H), 7.15-7.30 (m, 5H), 8.14 (s, 1H), 8.73 (s, 1H).

MS (ESI⁺) m / z: 449 [M+1]⁺ MS (ESI⁻) m / z: 447 [M-1]⁺

2-Chloro-N-[(\pm)-trans-3,7-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro -2H-1-benzopyran-6-yl]-acetamide

To a solution of

2-Chloro-*N*-[(±)-*trans*-3-hydroxy-7-methoxymethoxy-2,2-dimethyl-4-[(2-phenylethyl)a mino]-3,4-dihydro-2*H*-1-benzopyran-6-yl]-acetamide (228 mg, 0.51 mmol) in methylene chloride (6 mL), boron tribromide (1 M solution in methylene chloride, 2.42 mL, 2.42 mmol) was added at 0°C, and the resulting mixture was stirred for 2 hours. Upon the completion of the reaction, methanol and saturated aqueous sodium hydrogencarbonate solution were added thereto, and the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated aqueous sodium chloride solution, dried over magnesium sulfate and concentrated to obtain the aimed product (yield: 100%).

Colorless amorphous product

 $MS (ESI^{+}) m / z: 405 [M+1]^{+}$

MS (ESI) m / z: 403 [M-1]

(±)-trans-7-Hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-diox a-1-aza-anthracene-2-one

To a solution of

2-Chloro-*N*-[(±)-*trans*-3,7-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-1-benzopyran-6-yl]-acetamide (187 mg, 0.46 mmol) in methanol (2 mL), aqueous sodium hydroxide solution (1 mol/L, 1.8 mL) was added at room temperature, and the resulting mixture was stirred for 3 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with 1 mol/L aqueous sodium hydroxide solution and then with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (hexane/ethyl acetate = 1/3) and the aimed product was obtained (yield: 61%).

Colorless oily product

¹H-NMR (CDCl₃) δ: 1.14 (s, 3H), 1.45 (s, 3H), 2.65-3.00 (m, 4H), 3.53 (d. J = 9.9 Hz, 1H), 3.57 (d, J = 9.9 Hz, 1H), 4.50 (d, J = 15.4 Hz, 1H), 4.56 (d, J = 15.4 Hz, 1H), 5.99 (s, 1H), 6.40 (s, 1H), 7.15-7.40 (m, 5H). MS (ESI⁺) m / z: 369 [M+1]⁺

Synthesis Example 75

(±)-trans-6,6-Dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-az a-anthracene-7-ol maleate

(±)-trans-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza -anthracene-7-ol

To

(±)-*trans*-7-hydroxy-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,6,7,8-tetrahydro-4,5-dioxa -1-aza-anthracene-2-one (67 mg, 0.18 mmol), lithium aluminum hydride (1M solution in tetrahydrofuran, 910 μL, 0.91 mmol) was added at room temperature, and the resulting mixture was stirred at 90°C for 0.5 hour. Upon the completion of the reaction, saturated aqueous sod ium hydrogencarbonate solution was added thereto, the resulting solution was extracted with ethyl acetate, washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The resulting mixture was purified by silica gel column (ethyl acetate) and the aimed product was obtained (yield: 59%).

Colorless oily product

¹H-NMR (CDCl₃) δ: 1.13 (s, 3H), 1.43 (s, 3H), 2.75-3.00 (m, 4H), 3.30-3.35 (m, 2H), 3.50-3.70 (m, 2H), 4.15-4.25 (m, 2H), 6.12 (s, 1H). 6.25 (s, 1H), 7.20-7.35 (m, 5H). MS (ESI⁺) m / z: 355 [M+1]⁺

MS (ESI⁻) m / z: 389 [M+45]⁺ (HCOOH adduct)

(±)-trans-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza -anthracene-7-ol maleate

To a solution of

(±)-*trans*-6,6-dimethyl-8-[(2-phenylethyl)amino]-1,2,3,6,7,8-hexahydro-4,5-dioxa-1-aza -anthracene-7-ol in ethyl acetate (800 μ L), maleic acid (14 mg, 0.12 mmol) was added at room temperature, and the resulting mixture was stirred for 10 minutes. Hexane (1 mL) was added thereto, and the resulting mixture was stirred at 0°C for 30 minutes. The resulting crystal was filtered off and the aimed product was obtained (yield: 73%). Pale gray crystals

mp;162-162°C (decomposition)

¹H-NMR (DMSO-d₆) δ : 1.04 (s, 3H), 1.36 (s, 3H), 2.85-3.30 (m, 6H), 3.80-3.85 (m, 1H), 4.11 (d, J = 4.2 Hz, 2H), 4.**1** 5-4.20 (m, 1H), 6.05 (s, 2H), 6.18 (s, 1H), 6.76 (s, 1H), 7.20-7.40 (m, 5H).

Synthesis Example 76

 $(3R^*,4S^*)$ -4-{[2-(4-fluorophenyl)ethyl]amino}-7-hydroxymethyl-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

This compound was synthesized according to the process of Synthesis

Example 18. (Yield: 42%)

White crystals

mp;147-152°C

 1 H-NMR(CDCl₃); 1.26(s, 3H), 1.56(s, 3H), 2.59(s, 3H), 2.84-2.86(m, 2H), 2.92-3.09(m, 2H), 3.64(d, J = 10.5 Hz, 1H), 3.89(d, J = 10.2 Hz, 1H), 4.83(s, 2H), 6.99-7.05(m, 3H), 7.12-7.23(m, 2H), 7.29(s, 1H), 7.81(s, 1H)

MS(ESI*)m/z; 411 [M+1]*

MS(ESI⁻)m/z; 455 [M+45]⁺ (HCOOH adduct)

Synthesis Example 77

 $(3R^*,4S^*)$ -2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol 1 maleate

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

2,2-dimethyl-2*H*-pyrano[2,3-g]quinoline

Under nitrogen atmosphere, to a solution of 6-amino-2,2-dimethylchromene (3.88 g, 22.1 mmol) and ruthenium trichloride (55.0 mg, 0.265 mmol) in dimethylene glycol dimethyl ether (8 mL), 1,3-propanediol (0.639 mL, 8.84 mmol) and tri-*n*-butyl

phosphine (0.132 mL, 0.530 mmol) were added at room temperature, and the resulting mixture was stirred at 180°C for 5 hours. Upon the completion of the reaction, ruthenium complex was removed by florisil column, and solvent was distilled off. The residue was purified by medium pressure column chromatography (hexane/ethyl acetate =5/1) and the aimed product was obtained (yield: 59%).

Gray amorphous product

¹H-NMR(CDCl₃); 1.49(s, 6H), 5.91(d, J = 9.9 Hz, 1H), 6.59(d, J = 9.9 Hz, 1H), 7.08(s, 1H), 7.24-7.28(m, 1H), 7.67(s, 1H), 7.93(d, J = 8.0 Hz, 1H), 8.70(dd, J = 4.1 Hz, 1.7Hz, 1H)

MS(ESI⁺)m/z; 212 [M+1]⁺

 $(3R^*,4R^*)$ -3,4-epoxy-2,2-dimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline

This compound was synthesized according to the process of Synthesis Example 12.

(Yield: 65%)

CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 7.3 min.

Brown solid

 1 H-NMR(CDCl₃); 1.30(s, 3H), 1.65(s, 3H), 3.61(d, J = 4.4 Hz, 1H), 4.18(d, J = 4.4 Hz, 1H), 7.17(s, 1H), 7.34 (dd, J = 8.5 Hz, 4.4 Hz, 1H),8.01(d, J = 7.7 Hz, 1H), 8.12(s, 1H), 8.79(dd, J = 4.1 Hz, 1.7Hz, 1H)

MS(ESI⁺)m/z; 228 [M+1]⁺

 $(3R^*,4S^*)$ -2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

(Yield: 58%)

MS(ESI⁺)m/z; 349 [M+1]⁺

MS(ESI⁻)m/z; 393 [M+45]⁺ (HCOOH adduct)

(3R*,4S*)-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol 1 maleate

(Yield: 79%)

White crystals

mp;187-192°C (decomposition)

¹H-NMR(DMSO-d₆); 1.16(s, 3H), 1.50(s, 3H), 2.94-3.00(m, 1H), 3.09-3.20(m, 2H), 3.34-3.37(m, 1H), 4.07-4.11(m, 1H), 4.69(d, J = 9.4 Hz, 1H), 6.05(s, 2H), 6.32(br s, 1H), 7.23-7.39(m, 6H), 7.49(dd, J = 8.3Hz, 4.1 Hz, 1H), 8.22(d, J = 8.3 Hz, 1H), 8.44(s, 1H), 8.80(d, J = 3.9 Hz, 1H)

Synthesis Example 78

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(1-pyrrolidinyl)ethyl]amino}-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol

This compound was synthesized according to the process of Synthesis Example 19.

(Yield: 30%)

Orange amorphous product

¹H-NMR (CDCl₃) δ: 1.19 (s, 3H), 1.50 (s, 3H), 2.05-2.15 (br, 2H), 2.49 (s, 3H), 3.09-3.32 (m, 10H), 4.60-5.20 (br, 2H), 7.06 (s, 1H), 7.11 (s, 1H), 7.88 (s, 1H) MS (EI⁺) m / z; 390[M+1]⁺

Synthesis Example 79

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-{[2-(1,2,4-triazol-1-yl)ethyl]amino}-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

This compound was synthesized according to the process of Synthesis Example 19.

(Yield: 32%)

Pale yellow solid

¹H-NMR (CDCl₃) δ: 1.28 (s, 3H), 1.57 (s, 3H), 2.00 (br), 2.58 (s, 3H), 3.23-3.35 (m, 2H), 3.63 (d, J = 10.2 Hz, 1H), 3.90 (d, J = 10.2 Hz, 1H), 4.29-4.38 (m, 2H), 7.15 (s, 1H), 7.27 (s, 1H), 7.99 (m, 2H), 8.18 (s, 1H) MS (ESI⁺) m / z; 388 [M+1]⁺

Synthesis Example 80

 $(3R^*,4S^*)$ -7-hydroxymethyl-2,2,9-trimethyl-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol

This compound was synthesized according to the process of Synthesis Example 18.

(Yield: 38%)

Pale yellow crystals

¹H-NMR (CDCl₃) δ: 0.88-0.93 (m, 3H), 1.29 (s, 3H), 1.33-1.37 (m, 4H), 1.59 (s, 3H), 1.60 (m, 2H), 2.60 (s, 3H), 2.66-2.84 (m, 2H), 3.68 (d, J = 10.5 Hz, 1H), 3.94 (d, J = 10.5 Hz, 1H), 4.83 (s, 2H), 7.04 (s, 1H), 7.31 (s, 1H), 7.99 (s, 1H) MS (ESI⁺) m / z; 359[M+1]⁺

Synthesis Example 81

 $(3R^*,4S^*)$ -4-[(2-cyclopentylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinoxalin-3-ol

This compound was synthesized according to the process of Synthesis Example 59.

 $(3R^*,4S^*)$ -6,7-diamino-4-[(2-cyclopentylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-1-be nzopyran-3-ol

$$H_2N$$
 OH H_2N OH

Black amorphous product

 $(3R^*,4S^*)$ -4-[(2-cyclopentylethyl)amino]-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]qui noxalin-3-ol

¹H-NMR (CDCl₃) δ: 1.05(m, 2H), 1.31(s, 3H), 1.50-1.90(m, 9H), 1.59(s, 3H), 2.60-2.90(m, 2H), 3.37(brs, 1H), 3.68(d, J = 10.4 Hz, 1H), 3.93 (d, J = 10.4 Hz, 1H), 7.44 (s, 1H), 8.03 (s, 1H), 8.66 (d, J = 1.7 Hz, 1H), 8.74 (d, J = 1.7 Hz, 1H).

Synthesis Example 82

(3R*,4S*)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carboxylic acid

To a solution of

(3R*,4S*)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile described in Synthesis Example 14 (465 mg, **1**.20 mmol) in ethanol (5 mL), aqueous sodium hydroxide solution (3 mol/L, 5 mL) was added at room temperature, and the resulting mixture was stirred for 2 hours with reflux under

heating. After cooling to room temperature, the resulting solution was neutralized with 1 mol/L hydrochloric acid, precipitated brown solid was filtered off and the aimed product was obtained (yield: 90%).

Brown solid

¹H-NMR (CDCl₃) δ: 1.07 (s, 3H), 1.41 (s, 3H), 2.46 (s, 3H), 2.89-3.08 (br, 2H), 3.10-3.28 (br, 2H), 4.03-4.22 (br, 1H), 4.30-4.44 (br, 1H), 7.01-7.54 (m, 7H), 7.86 (s, 1H), 8.51-8.73(br, 1H) MS (El⁺) m / z; 407 [M+1]⁺

Synthesis Example 83

 $(3R^*,4S^*)$ -7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyr ano[2,3-g]quinolin-3-ol 2 maleate

 $(3R^*,4S^*)$ -7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyr ano[2,3-g]quinolin-3-ol

To a solution of

(3R*,4S*)-3-hydroxy-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-7-carbonitrile described in Synthesis Example 14 (110 mg, 0.283 mmol) in acetic acid (5 mL), 10% Pd/C (22 mg) was added at room temperature, and the resulting mixture was stirred for 2 hours under hydrogen atmosphere. Upon the completion of the reaction, the resulting solution was filtered through celite, the solvent was distilled off and then aqueous sodium carbonate solution was added to the residue, and the resulting solution was extracted with chloroform, dried over anhydrous magnesium sulfate, and the solvent was distilled off to obtain crude product of

 $(3R^*,4S^*)$ -7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyr ano[2,3-g]quinolin-3-ol (75.1 mg).

¹H-NMR(CDCl₃) δ ; 1.14(s, 3H), 1.46(s, 3H), 2.48(s, 3H), 2.73(t, J = 6.6 Hz, 2H),

2.88-2.95(m, 2H), 3.53(d, J = 10.5 Hz, 1H), 3.77(d, J = 10.2 Hz, 1H), 3.98(s, 2H), 7.04(s, 1H), 7.12-7.23(m, 6H), 7.84(s, 1H)

MS(ESI⁺)m/z; 392 [M+1]⁺

 $(3R^*,4S^*)$ -7-aminomethyl-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyr ano[2,3-g]quinolin-3-ol 2 maleate

(2-steps yield: 14%)

Brown crystals

mp:136-140°C

 1 H-NMR(DMSO-d₆) δ; 1.18(s, 3H), 1.49(s, 3H), 2.60(s, 3H), 2.90-3.00(m, 2H), 3.24-3.35(m, 2H), 4.02(brs, 1H), 4.33(s, 2H), 4.51(brs, 1H), 6.04(s, 4H), 7.21-7.42(m, 7H), 8.32(brs, 2H), 8.36(s, 1H)

Synthesis Example 84

 $(3R^*,4S^*)$ -9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol 1 maleate

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\$$

This compound was synthesized according to the process of Synthesis Example 18.

(2,2-Dimethyl-2H-pyrano[2,3-g]quinolin-9-yl)-methylacetate

To a solution of 2,2,9-trimethyl-2*H*-pyrano[2,3-g]quinoline described in Synthesis Example 1 (3.30 mg, 14.6 mmol) in chloroform (33 mL), a solution of *m*-chloroperbenzoic acid (5.54 g, 19.5 mmol) in chloroform (13.2 mL)-methanol (3.3 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, aqueous

sodium thiosulfate solution was added thereto and the resulting solution was extracted therewith. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetic anhydride (46 mL) was added to the residue at room temperature, and the resulting mixture was stirred at 150°C for 1 hour. Upon the completion of the reaction, acetic anhydride was distilled off, the residue was neutralized with aqueous sodium carbonate solution, extracted with chloroform, and the resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 1/1) and the aimed product was obtained (yield: 34%).

¹H-NMR(CDCl₃) δ; 1.41(s, 6H), 2.09(s, 3H), 5.37(s, 2H), 5.84(d, J = 9.9 Hz, 1H), 6.49(d, J = 9.9 Hz, 1H), 7.09(s, 1H), 7.24(d, J = 4.4 Hz, 1H), 7.66(s, 1H), 8.61(d, J = 4.4 Hz, 1H)

MS(ESI⁺)m/z; 284 [M+1]⁺

 $(3R^*,4R^*)$ -(3,4-epoxy-2,2-dimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-9-yl)-methyla cetate

(Yield: 58%)

99.5% ee; CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention time: 9.5 min.

Pale yellow solid

¹H-NMR(CDCl₃) δ 1.31(s, 3H), 1.66(s, 3H), 2.18(s, 3H), 3.62(d, J = 4.4 Hz, 1H), 4.18(d, J = 4.4 Hz, 1H), 5.47(d, J = 2.2 Hz, 2H), 7.28(s, 1H), 7.38(d, J = 4.1 Hz, 1H), 8.16(s, 1H), 8.78(d, J = 4.4 Hz, 1H) MS(ESl⁺)m/z; 300 [M+1]⁺

 $(3R^*,4S^*)$ -9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol

(Yield: 80%)

Brown amorphous product

¹H-NMR(CDCl₃) δ; 1.23(s, 3H), 1.52(s, 3H), 2.77-2.81(m, 2H), 2.90-3.04(m, 2H), 3.58(d, J = 10.5 Hz, 1H), 3.83(d, J = 10.4 Hz, 1H), 5.08(s, 2H), 7.17-7.21(m, 4H), 7.26-7.31(m, 2H), 7.44(d, J = 4.4 Hz, 1H), 7.98(s, 1H), 8.65(t, J = 4.7 Hz, 1H) MS(ESI⁺)m/z; 379 [M+1]⁺

MS(ESI)m/z; 423 [M+45] (HCOOH adduct)

 $(3R^*,4S^*)$ -9-hydroxymethyl-2,2-dimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2*H*-pyr ano[2,3-g]quinolin-3-ol 1 maleate

(Yield: 88%)

White crystals

mp;163-169°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 1.17(s, 3H), 1.50(s, 3H), 2.94-3.01(m, 1H), 3.09-3.21(m, 2H), 3.35-3.38(m, 2H), 4.09(dd, J = 9.6 Hz, 6.3 Hz, 1H), 4.72(d, J = 9.4 Hz, 1H), 4.91(s, 2H), 5.57(brs, 1H), 6.08(s, 2H), 6.34(d, J = 5.5 Hz, 1H), 7.23-7.39(m, 6H), 7.52(d, J = 4.4 Hz, 1H), 8.45(s, 1H), 8.77(d, J = 4.4 Hz, 1H)

Synthesis Example 85

 $(3R^*,4S^*)$ -2,2,9-trimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2H-pyrano[2,3-g]quino lin-3,7-diol 3/2 maleate

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

This compound was synthesized according to the process of Synthesis Example 18.

(2,2,9-Trimethyl-2*H*-pyrano[2,3-g]quinolin-7-yl)-acetate

To a solution of 2,2,9-trimethyl-2H-pyrano[2,3-g]quinoline described in Synthesis Example 1 (3.30 g, 14.6 mmol) in chloroform (33 mL), a solution of m-chloroperbenzoic acid (5.54 g, 19.5 mmol) in chloroform (13.2 mL)-me thanol (3.3 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 1 hour. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added thereto and the resulting solution was extracted therewith. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, acetic anhydride (46 mL) was added to the residue at room temperature, and the resulting mixture was stirred at 150°C for 1 hour. Upon the completion of the reaction, acetic anhydride was distilled off, the residue was neutralized with aqueous sod ium carbonate solution, extracted with chloroform, and the resulting organic p hase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by mediurn pressure column chromatography (hexane/ethyl acetate = 1/1) and the aimed prod uct was obtained (yield: 23%).

Red oily product

¹H-NMR(CDCl₃) δ; 1.49(s, 6H), 2.395(s, 3H), 2.404(s, 3H), 5.90(d, J = 9 .9 Hz, 1H), 6.58(d, J = 9.9 Hz, 1H), 7.23(s, 1H), 7.74(s, 1H), 8.48(s, 1H) MS(ESI⁺)m/z; 284 [M+1]⁺

 $[(3R^*,4R^*)\text{-}3,4\text{-epoxy-}2,2,9\text{-trimethyl-}3,4\text{-dihydro-}2H\text{-pyrano}[2,3\text{-}g]\text{quinolin -}7\text{-yl}]\text{-acetat}$ e

(Yield: 37%)

CHIRALPAK AD-RH 20 mM phosphate buffer (pH 8.0)/acetonitrile = 60/40, Retention

time: 6.6 min.

Brown amorphous product

¹H-NMR(CDCl₃) δ; 1.29(s, 3H), 1.64(s, 3H), 2.41(s, 6H), 3.60(d, J = 4.4 Hz, 1H), 4.15(d, J = 4.1 Hz, 1H), 7.31(s, 1H), 8.10(s, 1H), 8.47(s, 1H) MS(ESl⁺)m/z; 300 [M+1]⁺

 $(3R^*,4S^*)$ -2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-pyrano[2,3-g]quinoli n-3,7-diol

(Yield: 46%)

Brown amorphous product

 1 H-NMR(CDCl₃) δ; 1.25(s, 3H), 2.05(s, 3H), 2.48(s, 3H), 2.80(t, J = 6.6 Hz, 2H), 2.93-3.12(m, 2H), 3.58(d, J = 10.2 Hz, 1H), 3.84(d, J = 10.2 Hz, 1H), 7.12-7.25(m, 6H), 8.02(s, 1H), 8.66(s, 1H)

MS(ESI⁺)m/z; 379 [M+1]⁺ MS(ESI⁻)m/z; 377 [M-1]⁺

 $(3R^*,4S^*)$ -2,2,9-trimethyl-4-[(2-phenylethyl)amino)]-3,4-dihydro-2H-pyrano[2,3-g]quino lin-3,7-diol 3/2 maleate

(Yield: 70%)

White crystals

mp;184-188°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 1.16(s, 3H), 1.49(s, 3H), 2.35(s, 3H), 2.94-3.00(m, 1H), 3.10-3.22(m, 2H), 3.36-3.42(m, 1H), 4.04-4.10 (m, 1H), 4.66(d, J = 9.4 Hz, 1H), 6.12(s, 3H), 6.33(d, J = 5.8 Hz, 1H), 7.23-7.36(m, 6H), 8.30(s, 1H), 8.49(s, 1H), 10.12(s, 1H)

Synthesis Example 86

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-6 λ 5-oxy-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-p yrano[2,3-g]quinolin-3-ol hydrochloride

t-Butyl (2-phenylethyl)

[(3R*,4S*)-7-chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-yl] carbamate

To a solution of

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2*H*-pyrano[2,3-g]quinoline-3-ol described in Synthesis Example 19 (391 mg, 0.99 mmol) and di-*t*-butyl dicarbonate (430 mg, 1.97 mmol) in tetrahydrofuran (8 mL), triethylethylamine (600 μ L, 4.29 mmol) was added dropwise, and the resulting mixture was stirred at room temperature for 2 hours. Further, di-*t*-butyl dicarbonate (430 mg, 1.97 mmol) was added thereto at room temperature, and the resulting mixture was stirred overnight. Upon the completion of the reaction, aqueous sodium carbonate solution was added thereto and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 10/1) and the aimed product was obtained (yield: 87%).

MS(ESI⁺)m/z; 497 [M+1]⁺

MS(ESI)m/z; 541 [M+45] (HCOOH adduct)

t-butyl (2-phenylethyl)

[($3R^*$, $4S^*$)-7-chloro-3-hydroxy-2,2,9-trimethyl-6 λ 5-oxy-3,4-dihydro-2H-pyrano[2,3-g]qu inolin-4-yl] carbamate

To a solution of *t*-butyl (2-phenylethyl)

[(3R*,4S*)-7-chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-4-yl] carbamate (100 mg, 0.20 mmol) in chloroform (1 mL), a solution of *m*-chloroperbenzoic acid (75.9 mg, 0.44 mmol) in chloroform (0.4 mL)-methanol (0.1 mL) was added dropwise at room temperature, and the resulting mixture was stirred at room temperature for 30 minutes. At room temperature, a solution of

m-chloroperbenzoic acid (75.9 mg, 0.44 mmol) in chloroform (0.4 mL) was further added thereto and the resulting mixture was stirred overnight. Upon the completion of the reaction, aqueous sodium thiosulfate solution was added thereto and the resulting solution was extracted therewith. The resulting organic phase was washed with aqueous sodium hydrogencarbonate solution and then with aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by medium pressure column chromatography (hexane/ethyl acetate = 3/1 to 1/1) and the aimed product was obtained (yield: 41%). MS(ESI⁺)m/z; 513 [M+1]⁺

MS(ESI)m/z; 557 [M+45]* (HCOOH adduct)

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-6 λ 5-oxy-4-[(2-phenylethyl)amino)]-3,4-dihydro-2H-p yrano[2,3-g]quinolin-3-ol hydrochloride

To a solution of *t*-butyl (2-phenylethyl)

[$(3R^*,4S^*)$ -7-chloro-3-hydroxy-2,2,9-trimethyl-6 λ 5-oxy-3,4-dihydro-2H-pyrano[2,3-g]qu inolin-4-yl] carbamate (41.7 mg, 0.081 mmol) in 1,4-dioxane (0.2 mL), 4 mol/L hydrogen chloride-dioxane solution (0.42 mL) was added at room temperature, and the resulting mixture was stirred at 80°C for 1 hour. Upon the completion of the reaction, precipitated solid was filtered off and washed with di-isopropyl ether to obtain the aimed product (yield: 72%).

White crystals

mp;174-179°C (decomposition)

 1 H-NMR(DMSO-d₆) δ; 1.14(s, 3H), 1.49(s, 3H), 2.53(s, 3H), 3.00-3.55(m, 4H), 4.21(d, J = 9.1 Hz, 1H), 4.76(brs, 1H), 7.23-7.31(m, 6H), 7.45(s, 1H), 7.65(s, 1H), 9.08(s, 1H), 9.37(brs, 1H), 10.16(brs, 1H)

MS(ESI⁺)m/z; 413, 415 [M+1]⁺

MS(ESI⁻)m/z; 457, 459 [M+45]⁺ (HCOOH adduct)

Synthesis Example 87

 $(3R^*,4S^*)$ -7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-6 λ 5-oxy-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol hydrochloride

This compound was synthesized by using the compound of Synthesis Example 23 similarly to the process of Synthesis Example 86.

t-butyl [2-(4-fluorophenyl)ethyl]

 $[(3R^*,4S^*)$ -7-chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-yl] carbamate

MS(ESI⁺)m/z; 515, 517 [M+1]⁺

MS(ESI⁻)m/z; 559, 561 [M+45]⁺ (HCOOH adduct)

t-butyl [2-(4-fluorophenyl)ethyl]

[(3R*,4S*)-7-chloro-3-hydroxy-2,2,9-trimethyl-6 λ 5-oxy-3,4-dihydro-2H-pyrano[2,3-g]qu inolin-4-yl] carbamate

(2-steps yield: 30%).

MS(ESI⁺)m/z; 531, 533 [M+1]⁺

MS(ESI⁻)m/z; 575, 577 [M+45]⁺ (HCOOH adduct)

 $(3R^*,4S^*)$ -7-chloro-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2,9-trimethyl-6 λ 5-oxy-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol hydrochloride

(yield: 71%).

Pale yellow crystals

mp;193-198°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 1.14(s, 3H), 1.49(s, 3H), 2.53(s, 3H), 2.96-3.06(m, 1H), 3.16-3.18(m, 2H), 3.36(brs, 1H), 4.19-4.22(m, 1H), 4.75-4.78(m, 1H), 7.13(t, J = 9.08 Hz, 2H), 7.26-7.31(m, 2H), 7.45(s, 1H), 7.65(s, 1H), 9.06(s, 1H), 9.37(brs, 1H), 10.16(brs, 1H)

MS(ESI⁺)m/z; 431, 433 [M+1]⁺ MS(ESI⁻)m/z; 475, 477 [M+45]⁺

Synthesis Example 88

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-6 λ 5-oxy-4-pentylamino-3,4-dihydro-2*H*-pyrano[2,3-g]quinolin-3-ol hydrochloride

This compound was synthesized by using the compound of Synthesis Example 52 similarly to the process of Synthesis Example 86.

t-butyl (pentyl)

 $[(3R^*,4S^*)-7$ -chloro-3-hydroxy-2,2,9-trimethyl-3,4-dihydro-2H-pyrano[2,3-g]quinolin-4-yl] carbamate

MS(ESI*)m/z; 463, 465 [M+1]*

MS(ESI⁻)m/z; 507, 509 [M+45]⁺ (HCOOH adduct)

t-butyl (pentyl)

[(3R*,4S*)-7-chloro-3-hydroxy-2,2,9-trimethyl-6 λ 5-oxy-3,4-dihydro-2H-pyrano[2,3-g]qu inolin-4-yl] carbamate

(2-steps yields: 23%).

MS(ESI⁺)m/z; 479, 481 [M+1]⁺

MS(ESI⁻)m/z; 523, 525 [M+45]⁺ (HCOOH adduct)

 $(3R^*,4S^*)$ -7-chloro-2,2,9-trimethyl-6 λ 5-oxy-4-pentylamino-3,4-dihydro-2H-pyrano[2,3-g]quinolin-3-ol hydrochloride

(yield: 60%).

Pale yellow crystals

mp;226-230°C (decomposition)

¹H-NMR(DMSO-d₆) δ; 0.86(t, J = 6.3 Hz, 3H), 1.16(s, 3H), 1.27-1.29(m, 4H), 1.50(s, 3H), 1.60-1.72(m, 2H), 2.54(s, 3H), 2.86(brs, 1H), 3.07(brs, 1H), 4.07-4.10(m, 1H), 4.71(d, J = 8.5Hz, 1H), 6.51(d, J = 4.7 Hz, 1H), 7.47(s, 1H), 7.67(s, 1H), 9.04(s, 1H), 9.19(brs, 1H), 9.74(brs, 1H)

MS(ESI⁺)m/z; 379, 381 [M+1]⁺

MS(ESI⁻)m/z; 423, 425 [M+45]⁺ (HCOOH adduct)

Synthesis Example 89

 $(6S^*, 7R^*)$ -8,8-dimethyl-6-[(2-phenylethyl)amino)]-1,6,7,8-tetrahydrochromeno[7,6-e][1, 3,4]oxathiazin-7-ol 2,2-dioxide

t-Butyl (2-phenylethyl)

 $[(3R^*,4S^*)-7-\{[(chloromethyl)sulfonyl]amino\}-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2<math>H$ -1-benzopyran-4-yl] carbamate

To a solution of *t*-butyl (2-phenylethyl)

[(3R*,4S*)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2*H*-1-benzopyran-4-yl] carbamate described in Synthesis Example 71 (1.04 g, 2.35 mmol) in pyridine (1.90 mL, 23.5 mmol), chloromethanesulfonylchloride (0.31 mL, 3.52 mmol) was added, and the resulting mixture was stirred at room temperature for 10 hours. Upon the completion of the reaction, 1 mol/L aqueous hydrochloric acid solution (ca. 30 mL) was added thereto to adjust pH to about 7, and then the resulting solution was extracted with ethyl acetate, washed with saturated aqueous sodium chloride solution, and dried over anhydrous sodium sulfate and concentrated. The resulting mixture was purified by column chromatography (hexane/ethyl acetate = 3/1) and the aimed product was obtained (yield: 81%).

Colorless oily product

LC/MS (ESI⁺): 555[M+1]⁺ LC/MS (ESI⁻): 553[M-1]⁺

1-Chloro-N-{($3R^*$, $4S^*$)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

To a solution of *t*-butyl (2-phenylethyl)

[(3R*,4S*)-7-{[(chloromethyl)sulfonyl]amino}-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-di hydro-2*H*-1-benzopyran-4-yl] carbamate (400 mg, 0.72 mmol) in dichloromethane (4.0 mL), 1 mol/L solution of boron tribromide in dichloromethane (3.61 mL, 3.61 mmol) was added on ice bath, and the resulting mixture was stirred at 0°C for 1 hour. Water was added, and the resulting mixture was further stirred for 30 minutes. The resulting solid was filtered off, washed with water and then with chloroform. The solid was dried at 60°C for 3 hours under reduced pressure, and the aimed product

was quantitatively obtained.

LC/MS (ESI⁺): 441[M+1]⁺ LC/MS (ESI⁻): 439[M-1]⁺

(6S*,7R*)-8,8-Dimethyl-6-[(2-phenylethyl)amino]-1,6,7,8-tetrahydrochromeno[7,6-e][1, 3,4]oxathiazine-7-ol 2,2-dioxide

To a solution of

1-Chloro-*N*-{(*3R**, *4S**)-3,6-dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydr o-2*H*-1-benzopyran-7-yl} methanesulfonamide (220 mg, 0.50 mmol) in methanol (2.2 mL), 1 mol/L aqueous sodium hydroxide solution (1.00 mL, 1.00 mmol) was added, and the resulting mixture was stirred at room temperature for 3 hours. Then, the temperature was raised to 50°C, and the mixture was further stirred for 2 hours. Upon the completion of the reaction, the solution was cooled on standing, neutralized with saturated aqueous ammonium chloride solution, extracted 4 times with chloroform, and dried over anhydrous sodium sulfate. The solvent was distilled off and the aimed product was obtained (yield:37%).

Yellow solid

¹H-NMR (CDCl₃) δ : 1.13 (s, 3H), 1.44 (s, 3H), 2.54 (brs, 3H), 2.79-3.02 (m, 4H), 3.49 (d, J = 10.0 Hz, 1H), 3.59 (d, J = 10.0 Hz, 1H), 4.86 (s, 2H), 6.23 (s, 1H), 6.78 (s, 1H), 7.21-7.35 (m, 5H)

LC/MS (ESI⁺): 405[M+1]⁺ LC/MS (ESI⁻): 403[M-1]⁺

Synthesis Example 90

(±)-trans-6-Benzyl-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]indol-7-one

N-Benzyl-5-methoxyisatin

To a solution of 5-methoxyisatin (15.0 g, 84.7 mmol) in DMF (100 mL), sodium hydride (5.1 g, 127 mmol) and benzyl bromide (12.1 mL, 101.6 mmol) were added at 0°C, and the resulting mixture was stirred for 1 hour. Water was added thereto, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous ammonium chloride solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, and concentrated to obtain the aimed product (yield: 96%).

Brown solid

¹H-NMR(CDCl₃) δ; 3.77(s, 3H), 4.91(s, 2H), 6.67(d, J = 8.5 Hz, 1H), 7.0-7.1(m, 1H), 7.15 (m, 1H), 7.25-7.45(m, 5H)

N-Benzyl-5-hydroxyisatin

To a solution of *N*-benzyl-5-methoxyisatin (3.0 g, 11.2 mmol) in dichloromethane (60 mL), aluminum chloride (3.7 g, 28.1 mmol) was added, and the resulting mixture was stirred at 100°C for 1 hour. Water was added thereto, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, and concentrated to obtain the aimed product (yield: 78%).

Red solid

MS(ESI⁺)m/z; 254 [M+1]⁺ MS(ESI⁻)m/z; 252 [M-1]⁺

6-Benzyl-2,2-dimethyl-2H-pyrano[2,3-f]indole-7,8-dione

Under nitrogen stream, a solution of *N*-benzyl-5-hydroxyisatin (4.74 g, 18.7 mmol), potassium iodide (5.09 g, 31.8 mmol), potassium carbonate (5.17 g, 37.4 mmol), copper iodide (71 mg, 0.37 mmol) and 3-chloro-3-methyl-1-butyne (4.83 mL,

43.0 mmol) in DMF (47 mL) was stirred at 70°C for 2 hours. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, concentrated and purified by silica gel short column (chloroform).

1,2-dichlorobenzene (9 mL) was added and the resulting mixture was stirred ar 200°C for 30 minutes. After concentrating the reaction solution, the residue was purified by silica gel column (hexane/ethyl acetate = 5/1) to obtain the aimed product (yield: 8%). Red oily product

MS(ESI⁺)m/z; 320 [M+1] ⁺

6-Benzyl-2,2-dimethyl-2H-pyrano[2,3-f]indol-7-one

To a solution of 6-Benzyl-2,2-dimethyl-2*H*-pyrano[2,3-f]indole-7,8-dione (500 mg, 1.57 mmol) in DMF (5 mL), hydrazine monohydrate (2.5 mL) was added, and the resulting mixture was stirred at 100°C for 1.5 hour. Water was added thereto, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous ammonium chloride solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, concentrated and purified by silica gel column (hexane/ethyl acetate = 3/1) to obtain the aimed product (yield: 65%).

Yellow amorphous product MS(ESI*)m/z; 306 [M+1] *

(±)-trans-6-Benzyl-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydro-pyrano[2,3-f]indol-7-one

To 6-benzyl-2,2-dimethyl-2H-pyrano[2,3-f]indol-7-one (210 mg, 0.69 mmol) in chloroform-water mixed solution, sodium hydrogencarbonate (115 mg, 1.38 mmol) and *m*-chloroperbenzoic acid (237 mg, 1.38 mmol) were added, and the resulting mixture was stirred at room temperature for 3.5 hours. Aqueous sodium hydrogencarbonate solution and saturated aqueous sodium thiosulfate solution were added to the reaction solution, the resulting solution was extracted with chloroform, washed with saturated sodium chloride, dried over anhydrous sodium sulfate and

concentrated. 2-phenylethylamine (173 μ L, 1.38 mmol), lithium perchlorate (73 mg, 0.69 mmol) and dioxane (1 mL) were added to the resulting residue, and the resulting mixture was stirred at 70°C for 2 hours. Water was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with saturated aqueous sodium hydrogencarbonate solution and then with saturated sodium chloride solution, dried over anhydrous sodium sulfate, concentrated, purified by silica gel column (hexane/ethyl acetate = 1/1) and recrystallized with ethyl acetate to obtain the aimed product (2-steps yield: 16%).

Pale pink crystals

mp: 195°C (decomposition)

¹H-NMR(CDCl₃) δ; 1.16(s, 3H), 1.45(s, 3H), 2.8-3.2(m, 4H), 3.51 (s, 2H), 3.59(d, J = 4.4Hz, 1H), 3.73(m, 1H), 4.75(d, J = 15.7Hz, 1H), 4.84 (d, J = 15.7 Hz, 1H), 6.51 (s, 1H), 6.73 (s, 1H), 7.2-7.4(m, 10H).

MS(ESI⁺)m/z; 443 [M+1] ⁺

MS(ESI-)m/z; 441 [M-1]+

Synthesis Example 91

(±)-trans-4-{[2-(cyclohexa-1,3-dien-2-yl)ethyl]amino}3-hydroxy-2,2-dimethyl-2,3,4,6-tet rahydro-pyrano[2,3-f]indol-7-one

Under nitrogen stream, sodium (90 mg, 3.91 mmol) was added to liquid ammonia (5 mL) at -78°C, and the resulting mixture was stirred. A solution of (±)-trans-6-benzyl-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-2,3,4,6-tetrahydropyrano[2,3-f]indol-7-one (173 mg, 0.39 mmol) in THF (2 mL) was added dropwise at -45°C, and the resulting mixture was stirred for 15 minutes. Upon the completion of the reaction, saturated aqueous ammonium chloride solution was added thereto, the resulting solution was extracted with ethyl acetate. The resulting organic phase was washed with water and then with saturated sodium chloride solution, dried over anhydrous magnesium sulfate, concentrated and purified by silica gel column (ethyl acetate) to obtain the aimed product (yield: 19%).

White solid

¹H-NMR(CDCl₃) δ; 1.21(s, 3H), 1.49(s, 3H), 2.27(t, J = 6.9 Hz, 2H), 2.6-2.8(m, 4H),2.82-3.02(m, 2H), 3.44(m, 2H), 3.63(d, J = 4.4 Hz, 1H), 3.81 (d, J = 4.4 Hz, 1H), 5.54 (s, 1H), 5.74 (s, 2H), 6.72 (s, 1H), 6.86 (s, 1H), 8.78 (s, 1H).

[Preparation Examples]

Preparation Example 1

Tablet:

A compound according to the invention	10g
Lactose	260g
Microcrystalline cellulose	600g
Corn starch	350g
Hydroxypropyl cellulose	100g
CMC-Ca	150g
Magnesium stearate	30g
Total weight	1,500g

The aforementioned ingredients were mixed by a conventional method and then 10,000 sugar-coated tablets each containing 1 mg of the active ingredient per tablet were prepared.

Preparation Example 2

Capsule:

A compound according to the invention	10g
Lactose	440g
Microcrystalline cellulose	1,000g
Magnesium stearate	50g
Total weight	1,500g

The aforementioned ingredients were mixed by a conventional method and then filled into gelatin capsules to prepare 10,000 capsules each containing 1 mg of the active ingredient per capsule.

Preparation Example 3 Soft capsule:

A compound according to the invention	10g
PEG 400	479g
Saturated fatty acid triglyceride	1,500g
Peppermint oil	1g
Polysorbate 80	10g
Total weight	2,000g

The aforementioned ingredients were mixed by a conventional method and then filled into No. 3 soft gelatin capsules to prepare 10,000 soft capsules each containing 1 mg of the active ingredient per capsule.

Preparation Example 4 Ointment:

A compound according to the invention	1.0g
Liquid paraffin	10.0g
Cetanol	20.0g
White vaseline	68.4g
Ethylparaben	0.1g
1-menthol	0.5g
Total weight	100.0g

The aforementioned ingredients were mixed by a conventional method to obtain 1% ointment.

Preparation Example 5 Suppository:

A compound according to the invention	1g
Witepsol H15*	478g
Witepsol W35*	520g
Polysorbate 80	1g
Total weight	1,000g

(* trade name for triglyceride type compounds)

The aforementioned ingredients were melt-mixed by a conventional method, poured into suppository containers and cooled to solidify, and 1,000 suppositories (1g) each containing 1 mg of the active ingredient per suppository were prepared.

Preparation Example 6 Injection:

A compound according to the invention Distilled water for injection

1mg 5mL

It is used by dissolving when applied.

[Pharmacological Test Example]
Effects on the effective refractory period
Method

Beagles were anesthetized with pentobarbital sodium and thoracotomy was done along the median line under a respirator and the incision was made on the pericardium to expose the heart. An electrocardiogram (ECG) was recorded using bipolar electrodes attached to the surface of the right atrial free wall, right atrial auricle, and right ventricular free wall. The vagal nerves were stimulated using an electrostimulation device with Nichrome wires inserted into the vagal nerves in the neck bilaterally. The conditions for electrostimulation to the vagal nerves were set such that the RR intervals on ECG were prolonged by about 100msec compared with those before the stimulation was started.

Atrial and ventricular effective refractory periods were determined by S1-S2 extrastimulus technique at basic cycle length of 300 msec during bilateral vagal nerve stimulation, using programmable electric stimulator. A train of 10 basic stimuli(S1) was followed by a premature extrastimulus (S2) at 2 times diastolic threshold. The S1-S2 interval was successively decreased by 2 msec, and the effective refractory period was defined as the point at which S2 failed to produced a propagated response.

For evaluation of drug effects, the atrial and ventricular effective refractory periods were determined before drug administration, then respective compound was administrated intravenously at the dose of 0.3 mg/kg or 0.6 mg/kg, and the atrial and ventricular effective refractory periods were determined from 5 minutes after the administration.

The results were shown as the prolongation time on the atrial and ventricular effective refractory periods, i.e. [effective refractory period after drug administration] - [effective refractory period before drug administration] (msec).

Results

The compounds of the present invention exhibited the prolongation effect on the effective refractory period selective for atrium as shown in Table below.

Table

Synthesis Dose (mg/kg) Example No. (mg/kg)	Atrial Refractory Period (msec)	
		2
4	0.6	30
6	0.6	20
7	0.6	25
8	0.6	23
14	0.3	27
18	0.3	27
19	0.3	26
23	0.3	22
24	0.3	23
25	0.3	27
26	0.3	24
27	0.3	32
41	0.3	21
47	0.3	24
48	0.3	23
52	0.3	28
53	0.3	30
58	0.3	28
59	0.3	22
60	0.3	22
61	0.3	20
63	0.3	23
69	0.3	37
71	0.3	31
73	0.3	31
74	0.3	25
7 7 ·	0.3	25

Effects of the invention

The compounds according to the present invention exhibit the prolongation effect on the effective refractory period selective for atrium, thus can be used as an anti-atrial fibrillation agents and an supraventricular antiarrhythmic agent, and are useful as pharmaceuticals. Further, since the compounds according to the present invention have small influence on ventricle, they can contribute to safe treatments of aforementioned arrhythmic conditions.